

TITLE: 10023

Blood and urine exposure biomarkers as environmental surveillance tools for assessing military deployment exposures

AUTHOR:

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ABSTRACT:

This collaborative project will test newly developed blood and urine exposure biomarkers as environmental surveillance tools for assessing military personnel exposure to relevant military contaminants during military deployments. The objective of this research was to compare existing environmental exposure monitoring methods to new exposure biomarker methods by determining levels of volatile organic compounds, total and isotopic uranium, chemical agents, and heavy metals in the blood and/or urine of deployed troops pre-, during, and post deployment. Data from human specimens and environmental samples will be collected prospectively. Human specimens were compared internally and externally to national reference ranges published by the National Health and Nutrition Examination Survey. Environmental samples were used to determine correlations between external monitoring and exposure biomarker methods. Data collection was integrated with spatial (Geographical Information System) and epidemiological data for human populations. Once validated, this methodology will assess potential chemical health risks to future deployed forces and provide critical public health policy information.

10125 - Chromosomal Aberrations and Ionizing Radiation in Airline Pilots

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Airline pilots experience chronic low dose exposure to high energy galactic cosmic radiation. The purpose of this study was to quantify the cumulative effect of this exposure using a stable biological marker. Previous studies have shown an increased rate of transient chromosomal aberrations such as dicentrics and rings in crewmembers. However, dicentrics and rings decrease with time and thus do not serve as good indicators of cumulative exposure. Translocations may prove to be a better marker since they are relatively stable with time since exposure. This study quantified translocations in the blood of pilots and in a control group using fluorescent in situ hybridization (FISH), a technique for the rapid detection of structural chromosomal aberrations (translocations and insertions) in metaphase cells. Pilot volunteers were recruited from a single airline and controls were non-airline professionals. All volunteers were surveyed in regard to health status, family medical history, smoking history, current medications, and flight history. Based on this survey information, individuals were selected to provide blood samples. Selection criteria required that pilots and controls be as similar as possible except for flying history. All were healthy males, 40-60 years old, non-smokers, with no extensive medical exposure to radiation. The 40-60 year old age group was selected because it typically contains pilots with the most years flying experience. Frequent flyers among the controls were excluded. The cumulative galactic cosmic radiation dose in the pilot group was calculated using a computer program obtained from the US Federal Aviation Administration and flight history data from the survey. Individual pilot doses ranged from 26 to 72 millisieverts, with an average of 44 millisieverts. Findings from 11 pilots and 8 controls indicated a statistically significant difference between groups in the average number of translocations. The mean number of metaphases counted per subject was 2802 in the pilots and 3000 in the controls. Adjusting for genome equivalents, the mean percent translocations and standard error per group were as follows: pilots 0.91 ± 0.24 , controls 0.29 ± 0.09 , $p = 0.03$ (Mann-Whitney U test). Although pilots exhibited a three-fold increase over non-airline controls in the mean number of translocations detected, there was no indication within the pilot group of increasing translocation frequency with increasing radiation dose within the 26 to 72 millisievert range encountered in this study. The results of this study indicate that FISH is a suitable tool for the detection of accumulated chromosomal translocations in pilots.

MONITORING OF LEAD EXPOSURE IN SOME HIGH-RISK TARGET GROUPS IN ALBANIA

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Lead is an environmental pollutant of worldwide public health concern. High levels have been recently detected and reported in populations of some East European countries. The health effects of long-term low-level lead exposure have been extensively described and discussed in the literature. Recent studies have suggested a relationship between blood lead levels and neurological disturbances, elevated blood pressure, and a risk for cardiovascular disease.

As neonates, their mothers and young children constitute a most sensitive risk group, it was the aim of this study to determine cord-blood lead levels in neonates, blood levels in their mothers (by venipuncture), and finger-prick blood lead levels in preschool children living and attending kindergarten close to a source of lead emissions and of another group living and attending kindergarten in an urban area. During the period of the study we have also collected and analyzed air samples from three zones of Tirana.

Blood lead levels were measured in 188 neonates and their mothers, and in 152 preschool children; 59 air samples were taken. The analytical technique used to determine blood lead levels was *electrothermal atomic absorption spectrometry* (ETAAS); the laboratory performing these determinations participated in the external quality control activity during the survey.

Mean neonate blood lead levels were 13.1 $\mu\text{g Pb/dl}$ (range: 3.0–31.0 $\mu\text{g Pb/dl}$) and 15.1 $\mu\text{g Pb/dl}$ in their mothers (range: 3.3–39.2 $\mu\text{g/dl}$). The mean blood lead concentrations in children living and attending kindergarten close a source of lead emissions was 41.4 $\mu\text{g/dl}$ (range: 27.6–54.2 $\mu\text{g/dl}$), while in children living in an urban area it was 14.7 $\mu\text{g/dl}$ (range: 11.6–17.8 $\mu\text{g/dl}$). The mean air sample level was 0.115 $\mu\text{g/m}^3$ (range: 0.074–0.286 $\mu\text{g/m}^3$).

This study has demonstrated a very good (vertical transmission-type) correlation between maternal and neonatal umbilical chord blood lead levels ($y = 0.068 + 0.726 * x$ $r = 0.88$).

Also, a statistically significant difference ($p < 0.001$) was found between the blood lead levels of children living near and far from a lead pollution source. No correlation has been shown between air and blood lead levels.

10214 Synergistic effect by hepatitis virus infection and occupational chemical exposure on serum hepatic aminotransferase activity

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Abnormal hepatic aminotransferases have been associated with occupational chemical exposure and nonoccupational factors. However, interaction effects between occupational chemical exposure and non-occupational factors have not been clearly identified. We conducted a study to investigate the synergistic effect of occupational chemical exposure with hepatitis virus infection. The subjects included 568 male workers who worked in polyvinyl chloride (PVC) or vinyl chloride monomer (VCM) manufacturing factories, where workers were exposed to VCM and/or ethylene dichloride (EDC). Epidemiological information was obtained by an interviewer-administered questionnaire. Exposure levels of occupational chemicals were classified by hygienic exposure index (a summation of personal TWA / reference PEL of each chemical) into high, moderate and low exposure groups. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), and anti-hepatitis C antibody (anti-HCV) were assayed. Results revealed that hepatitis virus infection (positive HBsAg and/or positive anti-HCV) and increased body mass index were associated with abnormal hepatic aminotransferase activity. We also found that in workers with hepatitis virus infection, those with high exposure had a higher prevalence of abnormal AST and ALT as compared to low exposure group (OR=6.19, 95% CI=1.79-21.41; OR=6.45, 95% CI=1.77-23.56, respectively). Whereas, the prevalence of abnormal AST and ALT was not different between chemical exposure groups in workers without hepatitis virus infection. The interaction between chemical exposure (low, moderate, and high exposure group) and hepatitis B infection [HBeAg(-)/HBsAg(-), HBeAg(-)/HBsAg(+), and HBeAg(+)/HBsAg(+)] on AST and ALT were significant ($p < 0.01$). Among different combinations, those with positive HBeAg and high chemical exposure had highest risk of AST and ALT abnormality. We conclude that mixed exposure to EDC and VCM have an interaction effect with hepatitis B and C infection on liver damage. Those with hepatitis viral infection should be considered for their fitness for work when they have potential exposure to hepatotoxins.

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Afrim Tabaku

Public Health Institute Tirana, Albania

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10345 - Estimating exposure to Polycyclic Aromatic Hydrocarbons: a comparison of survey, biological monitoring and GIS-based methods

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Polycyclic aromatic hydrocarbons (PAHs) are produced during incomplete combustion of organic materials. Humans are exposed to these compounds from a variety of sources. Many PAHs are carcinogenic and readily absorbed through the skin, lungs and gastrointestinal tract. The objective of this study is to compare PAH exposure estimates, based on survey, biological monitoring and Geographic Information System (GIS) methods. We chose a convenience sample of 121 urban and 183 rural female members of the California Teachers Study cohort, residing in the greater SF Bay Area. The participants completed a survey about exposure to potential sources of PAHs within the last 48 hours and supplied a 24-hour urine sample. Urine samples were assayed for 1-hydroxypyrene-*O*-glucuronide (1-OHP), the major metabolite of pyrene, a common PAH. Survey data was collected regarding potential exposure to PAHs from tobacco, cooking, dietary sources, driving or traveling on roads and traffic levels around the home. A GIS was used to address geocode residence at the time of the survey and estimate traffic exhaust exposure using vehicle count data from the California Department of Transportation. ANOVA was conducted and Kruskal-Wallis test statistics calculated to determine if 1-OHP levels were related to self-reported potential sources of PAH exposure and to GIS-based estimates of traffic exposure. Cross tabulations and chi-square statistics were used to compare self-reported measures of traffic exposure to GIS-based measures of traffic exposure. Spearman rank correlation coefficients were used to evaluate the correlation between continuous exposure measures. Tobacco smoke appeared to have the largest influence on urinary 1-OHP measures ($p=0.01$). Subjects who reported smoking in the previous 48 hours had median concentrations (1.21 pmol/mL) nearly 10-fold that of non-smokers (0.16 pmol/mL). Further analyses of traffic-related and dietary determinants of 1-OHP were limited to non-smokers ($n=298$). Respondents who reported eating meat that was grilled, sauteed or broiled also had significantly higher 1-OHP levels ($p=0.02$). 1-OHP urine concentrations were elevated but not significant for those reporting exposure to environmental tobacco smoke and those living on streets with heavy or moderate vehicle traffic. Self reported living within 4 blocks of a highway or multi-lane road was not related to higher 1-OHP levels ($p=0.46$) and levels did not differ between urban and rural participants ($p=0.95$). Preliminary analyses revealed no correlation between the GIS-based traffic density estimates within a 1000 ft. radius of subjects' residences and their 1-OHP levels ($p=0.38$). Further analyses are being conducted to better account for dietary sources of PAHs as well as multivariate modeling to examine the most important predictors of 1-OHP concentrations.

CONTROLLED, SHORT-TERM DERMAL AND INHALATION EXPOSURE TO MTBE AND DIBROMOCHLOROMETHANE.Gordon, SM,¹ Brinkman, MC,¹ Satola, JR,¹ Wallace, LA,² Weisel, CE,³ and Shin, JY.³¹ Battelle Memorial Institute, Columbus, OH; ² U.S. Environmental Protection Agency, Reston, VA; ³ Environmental & Occupational Health Sciences Institute, Piscataway, NJ.

The oxygenate methyl tert-butyl ether (MTBE) has been added to gasoline to meet national ambient air quality standards in those parts of the US that are non-compliant for carbon monoxide. Although MTBE has provided important health benefits in terms of reduced hazardous air pollutants, the increasing occurrence and detection of MTBE in drinking water sources in California, New Jersey, and elsewhere has raised concerns about potential exposures from water usage and resulting health effects. In addition to MTBE, disinfection byproducts can be present in the water people use for showering, bathing, or drinking, as a result of the reaction of disinfection agents with organic material already present in water. Chlorine reacts with humic acids to form the trihalomethanes, which are the most common and abundant byproducts in chlorinated water. Besides chloroform, which has been widely studied, the byproduct dibromochloromethane (DBCM) occurs as a result of the chlorination process in those areas that naturally have bromide in their ground water. Relatively little information on exposure to this chemical is available. We conducted studies to determine the uptake by humans of MTBE and DBCM as a result of controlled, short-term dermal and inhalation exposures. Our approach made use of continuous real-time breath analysis to generate exhaled-breath profiles and evaluate MTBE and DBCM kinetics in the body. In the dermal exposure study, real-time breath analysis was used to measure the absorption of MTBE and DBCM while bathing in contaminated water. Seven subjects bathed in water containing MTBE-d₁₂ (at ~150 µg/L) and DBCM (at ~40 µg/L) at 40°C for 30 minutes. The breath profiles obtained for MTBE and DBCM were qualitatively similar to those for chloroform obtained in a previous study, but the amounts of MTBE and DBCM dermally absorbed were significantly lower than in the case of chloroform. In the inhalation study, seven subjects were exposed continuously to 500 ppb MTBE-d₁₂ and 115 ppb DBCM, except for several brief (2-min) intervals in which breath measurements were taken. Total exposure time was 30 min, followed by exposure to clean air for ~30 min. Exhaled breath was sampled and analyzed with the real-time breath technology; blood samples were simultaneously collected from the subjects (3-4 samples during exposure; 2-5 samples post-exposure). The real-time technology was specially modified with a biofeedback exposure control system to allow us to make uptake measurements during the exposure period; breath measurements were continuous throughout the post-exposure period. The uptake and decay of the target chemicals in the blood was estimated by fitting the exposure and post-exposure breath and blood data to a multi-compartmental model that estimated residence times. The measurements also provided information on blood:breath concentration ratios, as well as the fraction of breath MTBE and DBCM exhaled unchanged at equilibrium.

This work has been funded wholly or in part by the US Environmental Protection Agency under contract no. 68-D-99-011 to Battelle. The abstract has been subjected to Agency review and approved for publication.

10536 - USE OF METHOXYPHENOLS IN BIOLOGICAL AND ENVIRONMENTAL MONITORING OF WOODSMOKE EXPOSURE

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Epidemiological evidence indicates that air particulate matter (PM) is associated with adverse health effects including cardiovascular and respiratory impairment, leading to excess mortality and morbidity. Woodsmoke is a major source of PM in the Pacific Northwest. Therefore we have undertaken a substantial research effort to develop GC/MS-based methodology for quantitative analysis of particle-associated woodsmoke-derived methoxyphenols in ambient air samples. The target analytes include derivatives of guaiacol, syringol, eugenol and vanillin. We have also developed a GC/MS assay for determination of methoxyphenols in urine that provides a biomarker for exposure to atmospheric woodsmoke. An important feature of these assays is the inclusion of deuterium-labelled analogs of the methoxyphenols to control for analyte recovery. These methoxyphenol assays have been used to assess personal exposure to woodsmoke-derived fine particulate in an ongoing panel study of elderly subjects in the Seattle Metropolitan area. For each subject, over 10 consecutive days, PM_{2.5} samples were collected using personal samplers and fixed samplers located inside and outside the subject's residence. Each first daily urine void was collected over the 10 day sampling period also. We present data describing urinary methoxyphenol levels in a total of 300 urine samples, from 32 individuals. Up to 17 different methoxyphenols were detected in the urine samples, 12 of which were present in greater than 50% of the urine samples analyzed. The methoxyphenols were typically present at levels between 0.5-100 ng/mL. The limits of detection in urine samples were approximately 0.2 ng/mL. Methoxyphenols were also detected in ambient particulate samples, albeit at low levels. Several higher molecular weight compounds, including syringaldehyde and vanillin, were readily detectable in particulate samples (typical levels: 0.2-2 ng/m³, limits of detection 0.1-0.7 ng/m³), however many of the lower molecular weight compounds that were abundant in urine samples (e.g. syringol, eugenol), were infrequently detected in particulate samples. In conclusion, we have developed analytical methods to allow quantitative analysis of woodsmoke marker compounds (methoxyphenols) in human urine and ambient particles. The assays were applied in a study of exposure to ambient levels of woodsmoke, and the methoxyphenols were detected in both biological and environmental samples.

This work has been funded wholly by the United States Environmental Protection Agency under EPA co-operative agreement (#R827177) and the EPA Northwest Research Center for Particulate Air Pollution and Health (#R827355).

Validation of Whole Blood Cytokine Elicitation as a Biomarker for Organic Dust-Induced Inflammation

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Objectives: There is a need for improved methodology to assess responses to inflammatory agents in the environment. The whole blood assay (WBA) is a minimally invasive approach that may be a suitable alternative to nasal lavage or induced sputum analysis. The WBA measures cytokine production of circulating leukocytes after *ex vivo* stimulation with pro-inflammatory substances such as bacterial endotoxin (LPS). **Methods:** Male C3H/HeBFEJ mice were divided into 2 groups: sham (saline) exposure and dust-extract exposure. Mice were placed in a whole-body chamber and exposed by inhalation for 4 hr to a nebulized extract of dust collected from a concentrated swine feeding operation. Necropsies yielded whole blood and BAL fluid for total and differential leukocyte counts and IL-6 and TNF- α cytokine quantification. *Ex vivo* stimulants for the WBA were 170 EU/ml and 1700 EU/ml of endotoxin. Following an 18 hr incubation at 37°C and 5% CO₂, the WBA supernatants were tested for IL-6 and TNF- α cytokine production. **Results and Conclusions:** Inhalation exposures resulted in endotoxin concentrations of 153,000 EU/m³ of air and 2000 EU/mg of dust. The BAL revealed significantly higher total (1.44 million vs. 13,000 cells/mL) and neutrophil (3% vs. 96%) counts and cytokine responses between the sham and dust extract exposed groups. IL-6 increased by 56% and 53% over sham animals for the low and high LPS stimulation groups in the WBA. Experiments in progress use extracts of dust collected from different environments (municipal compost facilities and grass seed production facilities) and will test the effect of pre-exposure induced LPS tolerance on the WBA.

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Phenol, its Alkyl and Haloid Derivatives and Trihalomethanes Identification in Biological Media for the Problems of Monitoring of Tap Water Quality Health Effects

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Solving the problems of toxic organic substance control in water and human organism is important for water quality and health protection. Enterprises are the sources of phenol and its alkyl derivatives. Owing to imperfections of clearing structures, hazardous substances get into natural reservoirs and water supply system. Transformation of initial phenols into more toxic chlorphenol during tap water decontamination with available chlorine, and haloid formation (chloroform, tetrachlormethane, 1,2-dichlorethane, etc) are special problems. Study object is to develop high-sensitivity gas-chromatic methods of low concentration identification of study compounds in biological media. **1)**Development of gas-chromatic method of phenols and alkylphenols identification in urine and blood by their transformation into phenol derivatives - methylphenil ether (blood) and phenilacetate (urine) with further extraction with organic dissolvent. FID and stationary liquid phase –3%OV-1 were used as detectors. Degree of extraction for blood - 96.4%, for urine – 91%. Sensitivity of phenol identification in blood - $0.008 \mu\text{g}/\text{cm}^3$, error - 24.8%; in urine – $0.039 \mu\text{g}/\text{cm}^3$, error – 24.59%. To test this method health study of a group of 6-8 year children (25 persons) was carried. *Results of chemical analysis. Urine:* average – 0.12484 ± 0.02958 ($p < 0.05$); *blood:* average – 0.04402 ± 0.00941 , ($p < 0.05$). **2)**Development of gas-chromatic method for 2-chlorphenol identification in urine. Use of butylacetate extragent (pH=2), salting-out sodium chloride and ECD (20% camphor solution was added to extragent phase) was obtained to increase degree of extraction up to 95%. Sensitivity of 2-chlorphenol identification - $0.03 \mu\text{g}/\text{cm}^3$, error – 14.7%. To test this method health study of a group of 6-8 year children (25 persons) was carried. *Results of chemical analysis. Urine:* average – 0.42632 ± 0.15274 ($p < 0.05$). **3)** Development of methods for aliphatic chlorinated hydrocarbons identification in urine and blood. Maximum chloroform and 1,2-dichlorethane extraction from urine was obtained at extraction with heptane in acidic medium (pH=2). Degree of extraction - 94%. Sensitivity of chloroform identification in urine – $0.00005 \mu\text{g}/\text{cm}^3$, of 1,2-dichlorethane – $0.04 \mu\text{g}/\text{cm}^3$, of tetrachlormethane – $0.0005 \mu\text{g}/\text{cm}^3$, of chlorbenzene – $0.005 \mu\text{g}/\text{cm}^3$. Error for chloroform made 7%, for 1,2-dichlorethane – 20.3%, for tetrachlormethane – 24.7%, for chlorbenzene – 9%. There is maximum chloroform and tetrachlormethane extraction from blood at extraction with diethyl ether in alkaline medium (pH=8-10). Degree of extraction - 95%. Sensitivity of chloroform evaluation - $0.0006 \mu\text{g}$, for tetrachlormethane – $0.0001 \mu\text{g}$. Error for chloroform - 21.67%, for tetrachlormethane – 12.94%. The study of biological media for group of 6-8 year children (23 persons), living in the territories with central water-supply, was carried. *Results of chemical analysis. Urine:* chloroform – average 0.0061 ± 0.0015 ($p < 0.05$); tetrachlormethane – average 0.0020 ± 0.0001 ($p < 0.05$); 1,2-dichlorethane – average 0.0924 ± 0.0227 ($p < 0.05$); *blood:* chloroform – average 0.0059 ± 0.0017 ($p < 0.05$); tetrachlormethane – average

0.000008±0.000003 (p<0.05); 1,2-dichlorethane – average 0.043±0.017 (p<0.05).
Suggested methods make practical contribution to solution of procedure problem of
biological monitoring of study compounds in biological media.

Biological monitoring of low-level exposure to polychlorinated biphenyls from sealant material in schools

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Objectives: For many years, polychlorinated biphenyls (PCBs) have been a group of persistent pollutants with great importance in environmental medicine, especially because of their carcinogenic and suspected endocrine disrupting potential. Therefore, the release of PCBs from sealant material in concrete buildings has raised a great public debate in Germany about possible human health effects connected with this exposure. In a public school in Nuremberg, ambient monitoring of PCBs has revealed a high contamination, particularly with the more volatile low chlorinated PCB 28, PCB 52 and PCB 101.

This gave reason for a large biological monitoring study in order to examine the internal exposure to PCBs in pupils and teachers attending this building. Blood samples from 404 persons (median age: 12 years, range: 7 – 59 years) attending the PCB-contaminated school were drawn. 235 persons (median age: 11 years, range: 6 – 65 years) from a school with no detectable PCB-contamination served as a control group. To avoid any kind of bias, the blood samples were anonymised under supervision of a notary.

Methods: Using a highly sensitive method, serum samples were analysed for the six indicator PCBs (PCB 28, 52, 101, 138, 153, 180). Shortly, 2 ml of the serum sample were deproteinised using formic acid. The PCBs are then extracted with n-hexane, cleaned up on a silica gel column and finally quantified using gas chromatography with μ ECD-detection. Reagent blanks were included in every analytical series. Finally, the median reagent blank value plus the threefold standard deviation for every congener was subtracted from the results of the serum analyses.

Results: The results of our biological monitoring study are summarized in Table 1.

Congener		PCB-contaminated school (n=404)	control school (n= 235)
<i>PCB 28 [µg/l serum]</i>	median	0.007	n.d.
	95 th perc.	0.029	0.011
<i>PCB 52 [µg/l serum]</i>	median	0.010	n.d.
	95 th perc.	0.047	n.d.
<i>PCB 101 [µg/l serum]</i>	median	0.005	n.d.
	95 th perc.	0.032	0.008
<i>PCB 138 [µg/l serum]</i>	median	0.154	0.126
	95 th perc.	0.519	0.619
<i>PCB 153 [µg/l serum]</i>	median	0.196	0.164
	95 th perc.	0.744	0.877
<i>PCB 180 [µg/l serum]</i>	median	0.072	0.059
	95 th perc.	0.608	0.680

Table 1: Results of biological monitoring of persons attending a PCB-contaminated school and of a control school.

Conclusions: The results for the higher chlorinated PCBs are within the normal range of the general population for this age. Significant differences between both collectives were found concerning the lower chlorinated PCBs, especially for PCB 52. This is in excellent agreement with the results of air monitoring in the contaminated school. For the first time, it has been possible to quantify the excess internal exposure due to lower chlorinated PCBs in indoor air in a large collective.

Abstract

Title: 1 0672 - Current Status of the German External Quality Assessment Scheme (EQUAS) for Biological Monitoring in Occupational and Environmental Medicine

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Aim: External Quality Assessment Scheme (EQUAS) serves to improve the reliability of laboratory results by objectively testing their accuracy under analytical and medical requirements. Such programs must be also carried out for biological monitoring in occupational and environmental medicine to guarantee that the results are comparable with the threshold limit values and results from other laboratories.

Method: Since 1982 the German Society for Occupational and Environmental Medicine has offered 28 intercomparison programs. These programs cover 96 analytes in urine, blood, and plasma for 47 substances. These parameters are the most relevant in occupational and environmental medicine. The parameter spectrum includes:

Matrix	Parameter	Number of parameters	
		Environmental medicine	Occupational medicine
Blood	Metals	3	7
	Solvents		8
Urine	Inorganic compounds	6	16
	Organic compounds	9	19
Plasma	Organochlorine compounds	12	13
	Metals	10	

An additional pilot study was carried out for the determination of alkylphosphates in urine.

Results: The results of the intercomparison program 28, in which 167 laboratories from all over the world took part, showed that analyses of metals in blood and urine are requested most frequently. In the environmental range the determination of organochlorine compounds in plasma is of great importance. The results of the intercomparison program provide useful information on the present analytical quality of biological monitoring investigations. For the analyses of inorganic substances in blood and urine the tolerated variation ranges from 7,5% to 43,5%. For organic substances in urine, the tolerated variation ranges from 12% to 48%. The highest variation (36% to 60%) were found for the analyses of organochlorine compounds in plasma. The tolerated variations for determining solvents in blood by head space gaschromatography range from 26% to 57%. The percentage of successful determination is in the range from 30% to 74% for the various parameters. The overall average success rate for the participants of the external quality program range from 65% to 75%.

Conclusion: EQUAS are essential for the meaningful use of biological monitoring in occupational and environmental medicine. EQUAS objectively show the state of analytical art in biological monitoring and those diagnostic parameters which have to be improved with respect to their analytical reliability. Up to now in ambient monitoring like air, soil, dust analysis EQUAS of that size are missing.

10674 - Associations between atopic dermatitis and internal exposure to selected metals and organic chlorine compounds

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The prevalence of atopic dermatitis has increased within the last decades without a satisfying explanation for this phenomenon. One possible explanation, favored especially by doctors practicing alternative medicine is that rising prevalence of atopic dermatitis is caused by increasing environmental pollution. In psoriasis environmental causation is not discussed as prevalence of this condition has not changed over time.

In the presented study the internal exposure to lead, cadmium, mercury, platinum, arsenic as well as pentachlorophenol (PCP) and hexachlorobenzene (HCB) in blood or urine was assessed in 43 patients with atopic eczema. 41 controls with psoriasis were assessed respectively. Possible environmental influences were considered by taking a detailed environmental medical anamnesis including diet as well as lifestyle, housing, leisure and working conditions.

All substances never exceed the 95th percentile (reference values) of the German population. In an analysis of covariance associations between internal exposure to the analyzed pollutants and dermatological condition (atopic dermatitis/psoriasis) as well as substance specific influences (age, number of dental alloys, gender, smoking, consumption of fish, distance of home to a busy road) were studied. Age had an effect towards higher levels on PCP ($p=0.018$) and Pt ($p=0.002$) in urine, and HCB in blood ($p<0.0001$). Considering dental alloys a positive association was found between the number of amalgam fillings and Hg in urine ($p=0.0009$) and the number of dental gold inlays and Pt in urine ($p<0.0001$). Consumption of fish during the last 3 days was also strongly associated with the As levels in urine ($p=0.0006$). Gender seems also to influence the levels of Cd ($p=0.04$) in blood. Cd was the only parameter that was strongly influenced by smoking ($p=0.0001$). Psoriatic and not atopic dermatitis patients had higher levels of HCB ($p=0.026$) in blood.

This study confirmed known influences on internal human exposure of the pollutants analyzed and found internal exposures comparable to the German survey population. Furthermore internal exposure to environmental platinum and PCP was found to increase with age. Patients presenting with atopic dermatitis did not have higher internal concentrations of environmental pollutants. Therefore hypothesis of an environmental causation of atopic dermatitis is not supported by this study.

Exposure dependent change of liver detoxification capacity of children in former high loaded industrial areas

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Problem

The efficiency of remediation in early high loaded industrial areas is measured conventionally only by means of decreasing load. However, crucially is, to what extent the remediation or redevelopment contributes to an improvement of the health situation. The problem of a such argumentation is to provide a suitable physiological and/or biochemical parameter (effect-monitoring) or an indicator of exposure (biomonitoring) including the methods for the bio- and/or effect-monitoring.

Methods

Kindergarten children were selected from an industrial high polluted and a control area and watched under redevelopment for an epidemiologic cohort study to separate workplace-conditional and behavioural-conditional load (like smoking) against due to environmental factors changing exposure. It was investigated the region-specific external exposure with focus on organic chlorine compounds as well as the internal load (specific metabolites of the indicator components of the external exposure). The measurement of exposure has been done outdoors and indoors. Additional to the area specific exposure indicator components of air pollutants like sulfur dioxide and dust were registered over the time to get a outcome about the longterm common trend. With a specially developed diagnostic tool the liver detoxification capacity has been measured onhand of the elimination rate of an administered ¹⁵N-labelled drug ([¹⁵N]-Methacetin). Using the knowledge about the detoxification process of [¹⁵N]-Methacetin the amount of ¹⁵N labelled metabolites in urin are measured 6 hours after application. The test is highly sensitive and indicates an early deviation from expected „normal“ liver detoxification capacity

Results

The internal load with trichloro acetic acid (TCA) reflects the substantial difference in the exposure against chlorinated compounds especially tri- and tetrachloroethylene ($r=0.61$; $p < 0.05$). The load with trichloroethylene was 2 times, the load with chlororganic hydrocarbons in total 1.6 times higher in the loaded area compared with the control region. Children in the loaded area showed 7 % lower detoxification capacity compared with the control group. The improvement of the situation led to a about 35% reduced exposure which is expressed in improved liver detoxification capacity of the nonspecific cytochrome P450 system. The difference between loaded and control area was no more significant (difference in detoxification capacity 0.3%).

Discussion and conclusions

Chronical effect of xenobiotics in low concentrations can disturb the hepatic function. On stable isotopes based tools it is possible to characterize a health effect of multicomponent exposure considering the predominant pollutant. The proposed method is suitable for a

bioeffectmonitoring within the framework of screening and testing of the remediation efficiency.

10756 - Human exposure to uranium in drinking water:

Kenneth Orloff, Ketna Mistry, Paul Charp, Susan Metcalf - Agency for Toxic Substances and Disease Registry; Robert Marino, Tracey Shelley, Eric Melaro, Ann Marie Donohoe - South Carolina Department of Health and Environmental Control.

High concentrations of uranium were detected in water samples collected from private wells in a residential community. Using alpha radiation spectroscopy to quantitate individual isotopes, it was determined that the uranium contamination was from natural geological sources. Uranium concentrations in 36 wells ranged from 1.8 to 7,780 $\mu\text{g/L}$. (The drinking water MCL is 30 $\mu\text{g/L}$.) Urine samples were collected from 105 people 2 to 4 months after they had stopped drinking the water. The concentrations of uranium in these urine samples ranged from ND to 2.7 $\mu\text{g/g}$ creatinine, and 90 percent of the uranium concentrations exceeded the 90th percentile of a national reference population (0.024 $\mu\text{g/g}$). Statistical analyses indicated that the concentrations of uranium in the water and urine samples were significantly correlated. Six months later, a second urine sample was collected. Urine uranium concentrations were elevated in 90 percent of the people, although the concentrations decreased in most (63%) of the people tested. Urine uranium concentrations increased in some (37%) of the people tested. Most of these increases were small (less than 2-fold) and/or occurred in people with relatively low uranium concentrations. For the people with the highest urine uranium levels in the first investigation (> 1.0 $\mu\text{g/g}$), the urine uranium levels decreased an average of 78 percent over the 6-month time interval. At the time of the second investigation, a split urine sample was analyzed for retinol binding protein (RBP), an early marker of renal tubule damage. Although elevated RBP concentrations were detected in 3 of 79 people, there was no correlation between urine uranium concentrations and RBP concentrations. The results of this investigation suggest that long term exposure to uranium U in drinking water led to the accumulation of uranium in the body, which was slowly excreted in the urine. Ten months after exposure had ended, urine uranium levels were still significantly elevated.

10941 - Biological monitoring of exposure to pesticides : a comprehensive approach to internal dose measurements

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Synthetic pesticides have been used since in the early to mid twentieth century. In the U.S. alone, over 800 pesticide active ingredients are formulated in about 21,000 different commercial products. Although many public health benefits have been realized by the use of pesticides, their potential impact on the environment and public health is substantial.

Although epidemiologic studies have been conducted to determine if any relationship exists between pesticide exposure and disease, many lack integral components of the risk assessment equation. In the past several decades, researchers have proposed to fill these missing data gaps using biological monitoring of specific markers related to exposures. At CDC, we have worked to better define internal dose of pesticides using a repertoire of analytical methods that will allow for a comprehensive measure of exposure to both contemporary and organochlorine pesticides using highly selective and sensitive analytical techniques.

The methods we have developed are diverse in character but all use selective detection techniques and isotope dilution quantification. Our methods are precise, reliable and robust with limits of detection (LOD) that span a wide range. We have used these methods to measure pesticides and/or their metabolites in a variety of matrices including urine, serum, breast milk, saliva, and postpartum meconium. We present our comprehensive approach for biological monitoring of exposure to pesticides.

**11137 - Biomonitoring of Pulmonary Inflammation and Oxidative DNA Damage
Among Diesel Exposed Workers**

Burch JB, Bigelow P, Bakjaji K. Department of Environmental Health, Colorado State University, Fort Collins, CO 80523. Diesel exhaust exposures have been associated with reactive airway disorders, asthma, fibrotic lung disease, and lung cancer. Diesel exhaust, the largest source of suspended particulate matter in urban air, is comprised of a complex mixture of gases, carcinogenic and mutagenic organic chemicals, and a respirable carbon core (elemental carbon). These components may each contribute to diesel-induced lung cancer via pulmonary inflammation, the generation of reactive oxygen species, and the formation of oxidative DNA adducts. Biomonitoring approaches are needed to identify indicators of pathological pulmonary response to diesel exposures. This study tested the hypothesis that urinary excretion of the inflammation mediator, leukotriene E4 (LTE4), and the oxidative DNA adduct, 8-hydroxy-2'-deoxyguanosine (8-OHdG), was higher among transportation workers with elevated exposure to diesel exhaust constituents. The population consisted of 41 male bus mechanics, conductors, drivers and administrative workers in Damascus, Syria and Fort Collins, Colorado. Full-shift personal monitoring was performed for each participant to determine diesel-related gas (NO_x , CO_2 , CO) and particulate exposures (elemental, organic, and total carbon). Subjects provided post-shift and overnight urine samples on the same day as exposure assessment for analysis of LTE4 and 8-OHdG. A respiratory symptoms questionnaire was completed the following morning. Creatinine adjusted post-work and nocturnal urine concentrations, and total overnight excretion were calculated for LTE4 and 8-OHdG. Statistical analyses were performed by calculating adjusted (least-squares) mean LTE4 and 8-OHdG levels among workers with different diesel exposures using the generalized linear models (GLM) procedure in SAS. Nocturnal and overnight LTE4 concentrations were positively correlated with nighttime 8-OHdG excretion. Exposures were highest among workers in the Damascus bus depot, particularly bus mechanics. Syrian bus mechanics also had the highest levels of adjusted mean nocturnal LTE4 and 8-OHdG. There were no differences in post-work LTE4 or 8-OHdG levels among workers with high and low diesel exhaust exposures. The results suggest that elevated diesel exhaust exposures induce an inflammatory response in the lungs that contributes to increased urinary excretion of a marker of oxidative DNA damage.

11139 - Comparison of OP metabolite levels in single and multiple daily urine samples.

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A total organophosphate (OP) pesticide exposure study was conducted in Washington State in 1998. The sample population was 13 children aged 2.5 to 5.5 years. The children were roughly split between rural and suburban populations and had previously been identified as having potentially elevated OP exposures. One component of the study was urine collection and analysis. Urine samples were collected from each subject up to four times in 24 hours in two different seasons. Urine samples were analyzed initially for the six non-specific dialkylphosphate (DAP) metabolites and subsequently for eight specific metabolites including malathion dicarboxylic acid (MDA), 3,5,6-trichloro-2-pyridinol (TCPy) and paranitrophenol (PNP). Large percentages of the urine samples contained quantifiable amounts of at least two of the non-specific methyl-DAP metabolites (DMTP-95%; DMDTP-61%), one ethyl-DAP metabolite (DETP-65%), and three specific metabolites (MDA (72%), TCPy (82%) and PNP (94%)). The maximum observed concentration of any non-specific metabolite was 2 $\mu\text{mol/L}$ (DMTP) and the maximum observed concentration of any specific metabolite was 0.6 $\mu\text{mol/L}$ (TCPy). Creatinine concentrations were also determined and varied in individual samples by more than 80 fold. These data provide opportunity for examination of the consequences of alternative urine sampling strategies including the relative merits of multiple versus single (first-morning void) daily samples and the effect of creatinine adjustment on analytical results. At least qualitative comparison of correspondence between results obtained for specific and non-specific metabolites is also possible.

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