

10064-PM2.5 is more damaging to the biomolecules than PM10 because of more mobilized transition metals

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The mobilizable amount of transition metals is a fraction of the total amount of the metal from urban particulate matter. Although the fraction is small, some metals (Fe, Cu) are the major participants in a reaction that generates reactive oxygen species (ROS), which can damage various biomolecules. Damaging effects of the metals can be measured by the single strand breakage (SSB) of ϕ X174 RFI DNA or the carbonyl formation of protein. We hypothesized that the mobilizable fraction and thus the damaging effect of the metals be affected by the size of the dust particle. In another study, we have shown that more metals are mobilized by PM2.5 than by PM10 in general. However, it needs to show that more mobilized metals are more damaging to DNA and proteins since a metal can agonize or antagonize the effect of the other metal. PM2.5 and PM10 collected from a metropolitan area were employed. DNA SSB of >20% for PM2.5 and >15% for PM10 was observed in the presence of chelator (EDTA or citrate)/reductant (ascorbate), compared to the control (<3%) only with the chelator. The carbonyl formation by both PMs was very similar in the presence of the chelator, regardless of the kind of proteins. Compared to the control in the absence of chelator/reductant, 3.3 times and 4.9 times more carbonyl formation for PM2.5 and PM10, respectively, was obtained with BSA in the presence of chelator/reductant, showing that PM10 induced 33% more damage than PM2.5. However, 4.8 times and 1.9 times more carbonyl formation for PM2.5 and PM10, respectively, was observed with lysozyme in the presence of chelator/reductant, showing that PM2.5 induced 150% more damage than PM10. Although different proteins showed different sensitivities toward ROS, all these results indicate that the degrees of the oxidation of, or damage to, the biomolecules by the mobilized metals were higher with PM2.5 than with PM10. Therefore, it is expected that more metals mobilized from PM2.5 than from PM10, more damage to the biomolecules by PM2.5 than by PM10. We suggest that when the

toxicity of the dust particle is considered, the particle size as well as the mobilizable fraction of the metal should be considered in place of the total amount. This research was supported by a grant from the Ministry of Environment G-7 project, Korea.

10065-More transition metals are mobilized with PM2.5 than with PM10

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Fine air dust particles contain various transition metals (Fe, Cu, V, Co, Zn, Pb, etc.). When the dust particles are inhaled into the lung, some metals can participate in a reaction that generates reactive oxygen species (ROS), which could damage various biomolecules, such as DNA, lipid, and proteins. Other metals also can damage biomolecules in a variety of ways. However, within the lung or in biological fluids, not all the metals but a small fraction of the metals in the particles may be mobilized and take part in the generation of ROS. Additionally, the dust particle size may also influence the mobilization. Thus, the mobilization of the metal from particulate matters (PM2.5 and PM10 collected from metropolitan area) and SRM1648 (NIST, USA) was measured in the presence of 1mM of artificial chelator (EDTA, NTA, DTPA, HIMDA) or biological chelator (citrate, ATP, GTP) with or without reductant (ascorbate, cysteine, N-acetyl cysteine, or glutathione). The degree of the mobilization was higher with the artificial than with the biological chelator. However, the degree of the mobilization with the biological chelator was still much higher than control with 50mM of NaCl. The reductants increased the mobilization as much as about 5 times the control without them. Especially, the mobilization of Fe was greatly influenced by the presence of the reductant. Some metals showed noticeable difference between PM2.5 and PM10 in the mobilization of the metal. In case of Zn, the degrees of the mobilization with PM2.5 of spring and summer seasons were 1.5 and 2.0 times, respectively, higher than those with PM10. In case of Cu, the degrees of the mobilization with PM2.5 of summer and winter seasons were 1.5 and 25 times, respectively, higher than those with PM10. In case of Fe, the degree of the mobilization with PM10 of fall season was 1.5 times higher than that with PM2.5. In case of Pb, the degrees of the mobilization with PM2.5 of summer, fall, and winter seasons were about 2.0 times higher than those with PM10. All these results indicate that, in general, the degree of the mobilization of the transition metal is higher with PM2.5 than with PM10. Therefore, it is expected that, considering the previously known toxicities of the transition metals, the PM2.5 have a higher toxicity toward

various biomolecules than PM10. The results also suggest that not the total amount but the mobilizable fraction of the metal in the dust particles be considered as well as the particle size. This research was supported by a grant from the Ministry of Environment G-7 project, Korea.

10107-EPIDEMIOLOGICAL RISK ASSESSMENT: EARLY RECOGNITION OF RISKS AND IDENTIFICATION AND RANKING OF CRITICAL FACTORS

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The problem of early recognition of epidemiological risks and identification and ranking of critical factors, which determine rare events realisation take the central place in epidemiological risk analysis last years. Indeed, the Chernobyl disaster and events of September 11, 2001 have shown that even negligible value of risk can occur. So the theory of probability cannot be correctly utilised for risk assessment in some cases, when disaster has unique character. There is another approach to risk assessment, which may prove more useful here. In this approach the risk estimation is carried out using the theory of smooth functions allowing the determination of critical parameter values which describe the levels of control system intensities and reserve possibilities. The risk is estimated on a degree of the system parameter approximation of the bifurcation values, which characterise the system's transition from one steady state (norm), to another (catastrophe). This approach allows not only estimation of risk of emergency, but also description of the quantitative characteristic of reserve possibilities of the system and its components. The dynamics of these system parameters is determined with the help of dynamic modelling. The main advantage of this approach is the determination of risk dynamics as the function of dynamic variables of the investigated system. In this work the development of epidemiological and ecological situation in Ukraine is analysed with the help of aforementioned mathematical approach. The problems inherent in the optimum redistribution of resources with the purpose of maximising the efficacy of health care are examined. Optimisation problems were solved by a method of casual search. We considered multi-criterion statement of a problem to find an optimum control, which would permit to balance changes of parameters, describing different branches of epidemiological system, maximise the level of manufacture and quality of health care, on the one hand, and minimise epidemic risk and level of pollution, on the other. On the basis of this approach, the computer technology has been elaborated to support the solution of following tasks: 1) risk assessment of health deterioration connected with negative environmental impacts; 2) the ranking of some countries on risk of HIV/AIDS escalation; 3) the ranking of different regions of Ukraine on tuberculosis incidence rates; 4) infectious diseases dynamic forecasting and optimum redistribution of resources with the purpose of strengthening of management of infectious disease prevention and control efforts for maximization of efficacy post epidemic restoration; 5) ranking countries on their weakness, vulnerability and unpreparedness to possible bioterrorist attack and evaluation of capability to respond effectively to the threat of bioterrorism and to deal with consequences of terrorist attack.

10509-Prevalence of self-reported chemical sensitivity in central Germany

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Prevalence of and factors associated with self-reported chemical sensitivity in a middle sized town in Hesse a state in former West Germany was studied. Questions concerning chemical sensitivity, history of asthma and hay fever of the California Behavior Risk Factor Survey (BRFS, Kreutzer et al. 1999) were administered by telephone to subjects chosen randomly from the telephone registry. A questionnaire concerning environmental worry (Bowler et al. 1992, adapted for Germany by Hodapp et al. 1995) and questions concerning social status, education and smoking from the German Health Survey were applied.

The questions on chemical sensitivity were translated into German and retranslated to English by respective native speakers. 198 subjects were called up, 147 (74.2%) could be contacted following 3 trials and 100 (68,2%) participated.

The study population consisted of 55% females, 32% >30 years old, 69% having completed high school, 12% asthmatics. Not one reported a physician diagnosed multiple chemical sensitivity (MCS), nevertheless 24% considered themselves "allergic or unusually sensitive to everyday chemicals". 23% reported "unusual sensitivity to more than one type of chemical". In a logistic regression model including factors Kreutzer previously found to be associated with self-reported chemical sensitivity associations were found for asthma: adjusted odds ratio (OR) 4.28, 95% confidence interval (CI) 1.02-18.07 and females OR 4.61 CI 1.50-14.08 but not hay fever. When adjustment was extended to the sum score of environmental worry, association for females remained (OR 4.15, CI 1.32-12.98), while association for asthma disappeared (OR 3.78, CI 0.87-16.47). Environmental worry was not associated with self-reported chemical sensitivity.

Physicians diagnose of MCS, 6.3% in California in 1995, did not occur in the German study population of 2000/2001. Prevalence of sensitivity to more than one chemical on the other hand was markedly higher (23%) than in California (11.9%). This higher rate of self reported chemical sensitivity might be considered to result from a bias, since 2/3 of the study group was < 30 years and as many had completed high school. This bias seem unlikely though since age and education were not associated with self-reported chemical sensitivity in the large California survey. Higher rates in the German study group were also most likely not due to over reporting of subjects with higher general environmental worry, as it was not associated with self-reported chemical sensitivity.

As in the California survey, with comparable rates of females and asthmatics, associations between self-reported chemical sensitivity and gender as well as history of asthma were found.

Prevalence of self-reported chemical sensitivity in Germany was studied here for the first time allowing a comparison to prevalence in California. Although the rate of self reported chemical sensitivity was higher, physician diagnosed chemical sensitivity did not occur in the German study group. Like in California self-reported chemical sensitivity was associated with a history of asthma and with female gender. It could be shown here for the first time that chemical sensitivity is not associated with general environmental worry.

10542-QUANTITATIVE RISK ASSESSMENTS FOR A HOME HEALTH & SAFETY RATING SYSTEM

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BACKGROUND. A system of risk assessment is being developed for evaluating the fitness for habitation of residential properties in England. It is based on the estimation, mainly from epidemiological data, of the absolute health risk attributable to each of 28 specified hazards. Risk data for each hazard will be programmed into a hand-held computer as a practical decision aid for Environmental Health Officers. **METHODS.** Estimates of the risks associated with each home hazard were obtained in one of two ways. For hazards such as radon, asbestos and noise, exposure-risk relationships were obtained from published reviews. These exposure-risk relationships will be used in association with exposure measurements to obtain dwelling-specific annual probabilities of adverse health events. For other hazards, including accidents and cold (inadequate heating/insulation), attributable risks were estimated by linking routine data on mortality, hospital admissions and Accident and Emergency attendance to housing data from the English House Condition Survey and other small area statistics (Residata). The linkage was based on the postcode of residence (an average postcode contains 14 households). Excess risks were calculated for the most vulnerable group, and presented with and without adjustment for socio-economic status and other potential confounding factors. The main tabulations of risks were made by age of the property and whether or not they are in multiple occupation. For most hazards, dwellings in single occupation built since 1980 were taken as the baseline (lowest risk) group, and excess risks were calculated in relation to it. **RESULTS.** The results provide generally realistic and useful risk estimates for most home hazards. However, there are uncertainties in the attribution of risks to housing conditions for many of the hazards, and some of the risks appear to be large. For example, the results suggests that properties built before insulation standards were incorporated into building regulations are, on average, associated with greater than 1 in 10,000 annual probability of cold-related death for elderly residents. This would generally be considered an unacceptable level of excess risk. The risk of adverse health effects from carbon monoxide (CO) poisoning is estimated to be similarly high, especially in houses with older heating systems and if possible neuro-psychological effects of chronic CO exposure are considered. For CO, as for many hazards, case by case adjustments to the average risk (e.g. based on the condition of repair and maintenance of the boiler) would usually be needed to obtain a more individualized estimates of the risk associated with a particular property. **CONCLUSIONS.** The limited epidemiological evidence and uncertainties in attributing health risks to housing characteristics means that this approach to quantitative risk assessment can provide only a broad guide to housing fitness. Nonetheless, it represents a much needed systematic assessment of potentially important environmental risks associated with the housing stock.

10573-Neurotoxic effects of environmental agents: Data gaps that challenge dose-response estimation

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Dose-response estimation is a critical feature of risk assessment. It can be based on the results of epidemiologic, observational or clinical studies in humans and wildlife or laboratory-based animal studies. A systematic review of the epidemiologic literature on the potential neurotoxic effects of environmental agents was conducted. Effects have been relatively well described for lead across a spectrum of doses, but detailed dose-related information is generally lacking for other potentially neurotoxic compounds. In the example of methylmercury (MeHg), mental retardation, cerebral palsy and visual and auditory deficits have been observed in children of mothers exposed to high levels. At lower doses of MeHg exposure, a spectrum of functional deficits has been reported but the relation between dose and effect is less well understood. Other environmental agents such as polychlorinated biphenyls (PCBs) and related compounds, dioxins, pesticides, ionizing radiation, and environmental tobacco smoke have all been associated with adverse neurological and cognitive effects. With the exception of high dose ionizing radiation and PCB poisoning episodes, most observed effects for these agents have not included severe disability such as mental retardation, but have included poorer school performance and motor deficiencies. Among the maternal behavioral factors associated with neurotoxicologic effects, maternal alcohol, tobacco, marijuana and cocaine use were reviewed. For alcohol, the timing and conditions of exposure, as well as individual sensitivity of both the mother and fetus are important factors that moderate a potential dose-response relation. A spectrum of neurological effects is seen in infants exposed in utero to alcohol from serious disability to milder effects such as poor metacognition and learning difficulties. In general, it appears that neurotoxic effects of environmental exposures range in severity from mental retardation and disability to attention deficits, problems in school performance, and aggressive tendencies depending on the timing and dose of the chemical agent, but many potential neurotoxic agents have very little human data on low dose effects. Identifying the appropriate neurological and cognitive outcomes is essential to characterizing the dose-response relationship at lower levels of exposure. In epidemiological studies, the problems of selection bias, such as that observed in the investigation of low dose exposure to ionizing radiation following the detonation of the atomic bomb, and residual confounding, as in studies of environmental tobacco smoke exposure, must be overcome to adequately estimate the dose-response relationship. Both observational epidemiology and animal toxicology research efforts that focus attention on the neurotoxic effects of lower level environmental exposures are needed.

This is an abstract of a proposed presentation and does not necessarily reflect EPA policy.

10878-Effects of using exposure factors *a priori* normalized to body weight as input single variable, on the outcome of probabilistic risk assessments. Salinas, Julio A. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, Sacramento, California 95814.

The effects of dividing human exposure factors (e.g., breathing rate, ingestion rates, and dermal surface area) by body weight, and using the quotient as input probability density function (PDF) variable in probabilistic risk assessment (PRA), have been investigated. In PRA, the dose intake of contaminant at the point of contact is calculated by using Monte Carlo Simulation (MCS) statistical technique and algorithms that are specific for each exposure pathway and route of exposure. The MCS selects random values from each input PDF, conducts the calculations for all algorithms across contaminants and exposure pathways, incorporates the toxicity criteria, and generates an output PDF that reflects the range of health risks for the exposure scenario and receptor under consideration. While each simulation represents *one randomly sampled individual* from the population under study, with his/her respective randomly selected input exposure factors PDFs, the output PDF characterizes risk to that *population*. Because the overall dose intake is calculated by adding partial intakes across contaminants and exposure pathways, within each simulation the body weight is resampled every time with a new random value, as if a person could have one of each exposure factors but several different body weights. It also means that body weight is resampled many more times than each other exposure factor. This is conceptually wrong. *Each MCS should represent one virtual individual, and each associated input PDF should be randomly selected only once for that individual. Only then the MCS is a true simulation of individuals from a population, and the output result is a true representation of the range of individual risk estimates.* Some authors have suggested that if exposure factors normalized for body weight are used as input values, because of the multiple resampling of body weight (“multiple instantiations of single variable”) the resulting output PDF of dose or risk would have an erroneously smaller variance than expected, resulting in an under-representation of the extreme ends of the PDF. The error would result from the failure to recognize the covariance introduced in expressions that include the same variable. This hypothesis is unsupported, because when the exposure algorithms are rearranged in such a way that each input PDF variable appears only *once* for each individual in the same PRA example, results show that output uncertainty is the same for single or multiple resampling of body weight. However, *when I used exposure factors a priori normalized for body weights as input PDFs, the MCS generated output PDFs with increased uncertainty.* The basis and concerns about the use of this conceptual error will be presented, as well as the consequences on the uncertainty analysis, sensitivity analysis, and interpretation of the results. Risk assessors and risk managers are advised to correct this source of true uncertainty.

10896-RISK MANAGEMENT ACTIONS DIRECTED AT SOURCES OF ALDEHYDES TO INDOOR AIR IN CANADA.

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Under the Canadian Environmental Protection Act (CEPA), substances on the Priority Substances List (PSL) are assessed to determine whether exposure to them in Canada poses a risk to public health or to the environment. Three aldehydes (formaldehyde, acetaldehyde and acrolein) included on the PSL have been assessed, and been determined to pose a risk to public health, based on cancer/noncancer health effects and, for some, their contribution to formation of ground-level ozone. This determination sets the stage for the development of control options to reduce exposure to these substances. Common sources of these aldehydes to indoor air include emissions from tobacco smoking, building materials and furnishings, combustion appliances, high-temperature cooking with fats/oils, secondary formation from reaction of certain VOCs with ozone infiltrating from outdoors, and infiltration of outdoor air containing these aldehydes. Tobacco smoke is known to be a particularly important source of exposure to these substances, and a number of recent initiatives by the Tobacco Control Programme of Health Canada, including cigarette package labelling, emissions testing and reporting, and a national public health education campaign have focussed specifically on toxic substances, including some or all of the PSL aldehydes. Exposure to these aldehydes in indoor air will also be reduced as a result of some of the proposed risk management activities under CEPA that are directed at reducing its formation in the general environment. Hence, actions directed at residential wood combustion, such as those agreed to under the Canada-wide Standards for Particulate Matter and Ground-level Ozone, will serve to reduce indoor exposure from this source. In addition, other initiatives directed at reducing the levels of formaldehyde in outdoor air (including measures targetting emissions from on-road and off-road vehicles, and from the pulp and paper industry) will reduce exposure via infiltration of outdoor air into buildings. Background work being conducted for a number of the remaining indoor sources of these aldehydes, in order to characterize their potential contribution to public exposure and to examine possible measures to reduce exposure from these sources, will also be described.

11128-Ambient PAH Exposure and Cancer Risk: A meta-analysis

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INTRODUCTION: Polycyclic Aromatic Hydrocarbons (PAHs) are formed from the incomplete combustion of organic compounds. Major sources include vehicle emissions, domestic and industrial fossil fuel burning, environmental tobacco smoke and specific industrial processes. PAHs are present in the environment as complex mixtures. Specific compounds, e.g. benzo(a)pyrene (BaP), are established carcinogens. Several, mainly occupational, studies have identified relationships between PAH exposure and cancers of the lung and bladder. In order to combine evidence on exposure response functions for PAH and cancer and, in particular, to explore heterogeneity between studies, a review and meta-analysis of all relevant epidemiological studies was undertaken. Although of primary interest in assessing risks from occupational exposure, this also provides the only feasible basis for assessing risks from general environmental exposure. **METHODS:** Published studies from which exposure response relationships could be estimated were identified using electronic databases. Only studies in which PAHs were judged to be the predominant exposure to carcinogens were included. Almost half the selected studies had conducted exposure measurements within the plant, while exposures in the remainder were estimated from published values with the support of an industrial hygienist. For each study, relative risk increment per 100 $\mu\text{g}/\text{m}^3$ BaP years (RRI100) was estimated, assuming a linear model. Determinants of variation in RRI100s were investigated using random effect meta-regression techniques. **RESULTS:** Forty studies, nearly all occupational, were identified. Although the majority of studies found a positive association between PAH exposure and lung cancer risk, RRI100s ranged from less than zero to greater than 50. Preliminary analyses have found that neither industry, latency, confounder control, study design, or analysis method explain much of this variation. Some of the high and unstable RRI100s were from studies in occupations where PAH exposure was relatively low (e.g., in carbon black workers exposed to concentrations of 0.05 $\mu\text{g}/\text{m}^3$ BaP, compared to exposures of $\sim 15 \mu\text{g}/\text{m}^3$ BaP experienced by some Aluminium plant workers). Some of the highest stable RRI100s were reported from studies in China, while estimates from studies which provided exposure estimates within the coke oven and aluminium smelter industries conducted in Europe and the USA, were found to be broadly similar (RRI100 0.1, 0.3, 0.5, 0.5, 0.6, 0.8), with the exception of one (0.0; 95% CI: -0.2,0.1). Linear extrapolation from the median of these occupational studies suggests a lifetime lung cancer risk associated with current UK levels of ambient PAH (mean 0.13 ng/m^3 BaP) to be in the region of 18 per million. **CONCLUSION:** This work supports the established association of PAH exposure with lung cancer. However, there was a wide range of exposure response relationships. Although several of the largest studies were consistent with relative risks of around 1.5 for 100 $\mu\text{g}/\text{m}^3$ BaP exposure, outliers are, as yet, little explained. Higher RRI100s in studies from China, where smoking was less prevalent than in the west in the recent past, tentatively suggest the possibility of an additive effect of PAH exposure and smoking. Confounding by or interaction with general particulates has not yet been investigated.