

# Bulletin Board

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## CHEMICAL EFFECTS

### A review on the environmental exposure to airborne manganese, biomonitoring, and neurological/neuropsychological outcomes

2020-05-31

The occupational exposure to airborne manganese (Mn) has been linked for decades with neurological effects. With respect to its environmental exposure, the first reviews on this matter stated that the risk posed to human health by this kind of exposure was still unknown. Later, many studies have been developed to analyze the association between environmental Mn exposure and health effects, most of them including the measure of Mn in selected human biomarkers. This review aims at collecting and organizing the literature dealing with the environmental airborne Mn exposure (other routes of exposure were intentionally removed from this review), the biomonitoring of this metal in different body matrices (e.g., blood, urine, nails, hair), and the association between exposure and several adverse health effects, such as, e.g., neurocognitive, neurodevelopmental, or neurobehavioral outcomes. From the different exposure routes, inhalation was the only one considered in this review, to take into account the areas influenced by industrial activities closely related to the Mn industry (ferromanganese and silicomanganese plants, Mn ore mines, and their processing plants) and by traffic in countries where a fuel additive, methylcyclopentadienyl manganese tricarbonyl (MMT), has been used for years. In these areas, high air Mn levels have been reported in comparison with the annual Reference Concentration (RfC) given by the US EPA for Mn, 50 ng/m<sup>3</sup>. This review was performed using Scopus and MEDLINE databases with a keyword search strategy that took into account that each valid reference should include at least participants that were exposed to environmental airborne Mn and that were subjected to analysis of Mn in biomarkers or subjected to neurological/neuropsychological tests or both. Overall, 47 references matching these criteria were included in the discussion. Most of them report the measure of Mn in selected biomarkers (N = 43) and the assessment of different neurological outcomes (N = 31). A negative association is usually obtained between Mn levels in hair and some neurological outcomes, such as cognitive, motor, olfactory, and emotional functions, but not always significant. However, other biomarkers, such as blood and urine, do not seem to reflect the chronic environmental exposure to low/moderate levels of airborne Mn. Further studies

In these areas, high air Mn levels have been reported in comparison with the annual Reference Concentration (RfC) given by the US EPA for Mn, 50 ng/m<sup>3</sup>.

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combining the determination of the Mn exposure through environmental airborne sources and biomarkers of exposure and the evaluation of at least cognitive and motor functions are needed to better understand the effects of chronic non-occupational exposure to airborne Mn.

Authors: Ignacio Fernández-Olmo, Paula Mantecón, Bohdana Markiv, Laura Ruiz-Azcona, Muguel Santibáñez

Full Source: Review of environmental contamination and toxicology. 2020 May 31. doi: 10.1007/398\_2020\_46. Online ahead of print.

### Pulmonary toxicity of silver vapours, nanoparticles and fine dusts: a review

2020-05-28

Silver is used in a wide range of products, and during their production and use, humans may be exposed through inhalation. Therefore, it is critical to know the concentration levels at which adverse effects may occur. In rodents, inhalation of silver nanoparticles has resulted in increased silver in the lungs, lymph nodes, liver, kidney, spleen, ovaries, and testes. Reported excretion pathways of pulmonary silver are urinary and faecal excretion. Acute effects in humans of the inhalation of silver include lung failure that involved increased heart rate and decreased arterial blood oxygen pressure. Argyria—a blue-grey discoloration of skin due to deposited silver—was observed after pulmonary exposure in 3 individuals; however, the presence of silver in the discolorations was not tested. Argyria after inhalation seems to be less likely than after oral or dermal exposure. Repeated inhalation findings in rodents have shown effects on lung function, pulmonary inflammation, bile duct hyperplasia, and genotoxicity. In our evaluation, the range of NOAEC values was 0.11-0.75 mg/m<sup>3</sup>. Silver in the ionic form is likely more toxic than in the nanoparticle form but that difference could reflect their different biokinetics. However, silver nanoparticles and ions have a similar pattern of toxicity, probably reflecting that the effect of silver nanoparticles is primarily mediated by released ions. Concerning genotoxicity studies, we evaluated silver to be positive based on studies in mammalian cells in vitro and in vivo when considering various exposure routes. Carcinogenicity data are absent; therefore, no conclusion can be provided on this endpoint.

Authors: Niels Hadrup, Anoop K Sharma, Katrin Loeschner, Nicklas R Jacobsen

Full Source: Regulatory toxicology and pharmacology: RTP. 2020 May 28;104690. doi: 10.1016/j.yrtph.2020.104690. Online ahead of print.

In rodents, inhalation of silver nanoparticles has resulted in increased silver in the lungs, lymph nodes, liver, kidney, spleen, ovaries, and testes.

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## ENVIRONMENTAL RESEARCH

## Occurrence of halogenated pollutants in domestic occupational indoor dust

2020-05-27

The occurrence of halogenated organic pollutants in indoor dust can be high due to the presence of textile, electronic devices, furniture, and building materials treated with these chemicals. In this explorative study, we focused on emerging organic pollutants, such as novel brominated flame retardants (nBFRs) and some perfluoroalkyl substances, together with legacy polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (BDEs) in settled dust collected in houses and workplaces such as one office and two electrotechnical and mechanical workshops. The total contribution of the investigated pollutants was lower in house and in office dusts except for few nBFRs (such as bis (2-ethylhexyl)-3,4,5,6-tetrabromo-phthalate at a concentration of 464.5 ng/g in a house and hexachlorocyclopentadienyldibromocyclooctane at 40.4 ng/g in the office), whereas in electrotechnical and mechanical workshops a high incidence of PCBs, BDEs, and nBFRs occurred (for example, BDE 209 at a concentration of 2368.0 ng/g and tetrabromobisphenol A at 32,320.1 ng/g in electrotechnical and mechanical workshops). Estimated daily intakes were also calculated, showing that domestic and occupational environments can lead to a similar contribution in terms of human exposure. The higher exposure contribution was associated to nBFRs, whose EDIs were in the range of 3968.2-555,694.2 pg/kg bw/day. To provide a complete view about the indoor contamination, in this investigation, we also included polycyclic aromatic hydrocarbons (PAHs) and their oxygenated and nitrated derivatives. Definitely, dust collection represents a simple, fast, and cost-effective sampling and dust contamination level can be a useful indicator of environment healthiness. Besides, the presented method can be a smart tool to provide a time and money saving technique to characterize 99 pollutants thanks to a single sample treatment.

Authors: Giulia Simonetti, Patrizia Di Filippo, Carmela Riccardi, Donatella Pomata, Elisa Sonogo, Francesca Buiarelli

Full Source: International journal of environmental research and public health. 2020 May 27;17(11):E3813. doi: 10.3390/ijerph17113813.

Estimated daily intakes were also calculated, showing that domestic and occupational environments can lead to a similar contribution in terms of human exposure.

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## Study protocol to examine the relationship between environmental exposure to lead and blood lead levels among children from day-care centres in Ekurhuleni Metropolitan Municipality

2020-05-30

Introduction: Lead exposure is toxic to all humans and is very harmful to young children, especially 5-year-olds. Elevated blood lead levels (BLLs) in children have been associated with their daily surrounding environment. This protocol seeks to evaluate the association between environmental lead exposure and BLLs among children in day-care centres, including household and other risk factors.

Methods and analysis: To achieve the objectives of the study, we adopted a cross-sectional analytical design. A portable X-ray fluorescence analyser was used for environmental sampling, and BLLs were determined using the LeadCare II machine among preschool children. Household and other risk factors were assessed using a questionnaire. Random sampling was employed to select day-care centres in the municipality and children in each day-care centre. Data will be analysed using SPSS V. 26. Ethics and dissemination: Ethical approval and permission were obtained prior to commencement of the study. The researcher intends to publish the results in peer-reviewed journals and also to present a paper at a scientific conference. The study will generate information on environmental lead exposure among vulnerable children (2-5 years), and it will promote public health action to prevent long-term exposure in day-care centres.

Keywords: blood lead levels; day-care centres; environment; environmental health; household risk factors; short-term lead exposure.

Authors: Mbalenhle Desiree Cindi, Thokozani Patrick Mbonane, Nisha Naicker

Full Source: BMJ Open. 2020 May 30;10(5):e036687. doi: 10.1136/bmjopen-2019-036687.

This protocol seeks to evaluate the association between environmental lead exposure and BLLs among children in day-care centres, including household and other risk factors.

## Photodegradation of 1,3,5-Tris-(2,3-dibromopropyl)-1,3,5-triazine-2,4,6-trione and Decabromodiphenyl Ethane flame retardants: kinetics, main products, and environmental implications

2020-05-20

Photodegradation has been demonstrated as one of the important environmental factors affecting the fate of contaminants such as

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brominated flame retardants (BFRs). However, a number of emerging BFRs, particularly those with high bromine substitution, have rarely been investigated for their photodegradation kinetics. Our study evaluated photodegradation of two highly brominated FRs, 1,3,5-tris-(2,3-dibromopropyl)-1,3,5-triazine-2,4,6-trione (TDBP-TAZTO) and decabromodiphenyl ethane (DBDPE), under various conditions. The results indicated that the degradation kinetics was affected by UV irradiation wavelength, intensity, solvent type, as well as the structural characteristics. TDBP-TAZTO exhibited degradation half-lives ( $t_{1/2}$ ) of 23.5-6931 min under various UV irradiation conditions and 91.2 days under natural sunlight. Its degradation was much slower than that of DBDPE which exhibited  $t_{1/2}$  of 0.8-101.9 min under UV and 41.3 min under natural sunlight. A variety of degradation products were detected as a result of different breakdown pathways. This indicated that photodegradation could substantially influence the fate of these highly brominated FRs, resulting in a cocktail of degradation products as environmentally occurring contaminants. This could also complicate the evaluation of the ecological risks of these target flame retardants, given that degradation products generally possess physicochemical properties and biological effects different from their parent chemicals.~sAuthors: Daming Zhou, Xiaoshi Zheng, Xiaotu Liu, Yichao Huang, Weijie Su, Hongli Tan, Yan Wang, Da Chen  
Full Source: Journal of hazardous materials. 2020 May 20;398:122983. doi: 10.1016/j.jhazmat.2020.122983. Online ahead of print.

## PHARMACEUTICAL/TOXICOLOGY

### Instability of urinary excreted methyl-2-acetamido-2-deoxy-1-seleno- $\beta$ -d-galactopyranoside (Selenosugar 1), the main elimination product of human selenium metabolism, and measures for its stabilisation

2020-05-05

Background: The urinary excreted selenium species selenosugar 1 (SeSug1) plays a key role for monitoring of supplemental selenium exposure, e.g. by occupational exposure. In order to reproduce its contents in the long term, the integrity of SeSug1 in the urine is essential. Studies on the stability of SeSug1 in urine samples stored at -20 °C have shown that degradation of SeSug 1 occurs, requiring adequate countermeasures. Methods: Here, we explored the long-term stability of SeSug1 under usual storage conditions at -20 °C. For this purpose, the simultaneous determination of selenosugar 1 and methylselenic acid (MeSeA) was

Here, we explored the long-term stability of SeSug1 under usual storage conditions at -20 °C.

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used to explore the stabilizing of the SeSug1 content by applying sodium azide ( $\text{NaN}_3$ ) as a bactericide or/and 5 M ammonium acetate buffer for pH control.

Results: In untreated urine, conversion of SeSug1 to MeSeA was evident within days. Differences in urine matrices clearly showed different impact, which could be attributed to different buffer strengths by the urine itself. For durability, various concentrations of sodium azide were first applied, followed by pH buffering. A combination of 0.1%  $\text{NaN}_3$  and pH of 5.5 kept the SeSug1 content stable for over 3 months.

Conclusion: The formation of MeSeA as degradation product of SeSug1 could be confirmed. Based on the proportions, an oxidation-based decomposition pathway was proposed. The investigations revealed that the complex interaction of pH buffering and bactericidal activity must be taken into account in order to stabilize SeSug1 in the urine. The main effect was the addition of  $\text{NaN}_3$ . However, the alkaline nature of  $\text{NaN}_3$  required a sufficient buffering of the urinary matrix at a pH of 5.5.

Authors: Jörg Hildebrand Thomas Göen

Full Source: Journal of trace elements in medicine and biology: organ of the society for Minerals and Trace Elements (GMS)

### Perfluoroalkyl substances exposure and hearing impairment in US adults

2020-05-18

Background: Per- and polyfluoroalkyl substances (PFAS) are widely applied in consumer and industrial products such as nonstick cookware, waterproof clothing, food packaging materials, and fire-fighting foams. These "forever chemicals" are hypothesized to impact neurobehavioral functions. Yet no previous study has explored the role of PFAS on audiometrically determined hearing impairment (HI).

Objectives: To investigate the associations of serum concentrations of perfluoroalkyl substances with low-frequency HI (LFHI) and high-frequency HI (HFHI) in US adults.

Methods: We evaluated the cross-sectional associations in 2371 adults aged 20-69 years who participated in the National Health and Nutrition Examination Survey (NHANES) 2003-2004, 2011-2012 and 2015-2016; and 449 adults aged  $\geq 70$  years from NHANES 2005-2006 and 2009-2010. Serum concentrations of perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA), were measured using solid-phase extraction coupled to High Performance Liquid Chromatography-Turbo Ion Spray ionization-tandem Mass Spectrometry.

These "forever chemicals" are hypothesized to impact neurobehavioral functions.

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LFHI was defined as a pure-tone average (PTA) of thresholds across 0.5-1-2 kHz >25 dB; HFHI defined as a PTA across 3-4-6 kHz >25 dB in the worse ear. Survey-weighted logistic regression models were used to compute odds ratios (ORs) and 95% confidence intervals (CIs) with adjustment for age, age-squared, sex, race/ethnicity, education, poverty-to-income ratio, body mass index, smoking status, exposures to occupational, recreational and firearm noises, and NHANES cycles.

Results: There were no significant associations when perfluoroalkyl variables were fitted as a linear (log-transformed) term. However, statistically significant associations of HFHI with PFNA (OR = 1.70, 95% CI: 1.13-2.56) and PFDA (OR = 1.75, 95% CI: 1.00-3.05) were observed when comparing participants with serum concentrations  $\geq$ 90th vs. <90th percentiles of PFNA (90th percentile = 1.8 ng/mL) and PFDA (90th percentile = 0.5 ng/mL), respectively, in adults aged 20-69 years. No significant associations were observed for other compounds in adults aged 20-69 years and for all compounds in adults  $\geq$ 70 years.

Conclusions: Our study does not provide strong evidence to support the ototoxicity of PFAS exposure. Non-linear threshold dose-response associations between serum concentrations of PFNA and PFDA and HFHI need further investigation.

Authors: Ning Ding, Sung Kyun Park

Full Source: Environmental research. 2020 May 18;187:109686. doi: 10.1016/j.envres.2020.109686. Online ahead of print.

### Associations between essential metals exposure and metabolic syndrome (MetS): Exploring the mediating role of systemic inflammation in a general Chinese population

2020-07-01

Background: Essential metals have been reported to be associated with metabolic diseases. However, the relationships between essential metals exposure and Metabolic Syndrome (MetS) is still uncertain, and the underlying mechanisms of the association remain unclear.

Objectives: To investigate the associations of urinary essential metals with MetS prevalence; and further to explore potential role of systemic inflammation biomarker, C-reactive protein (CRP), in relationships between essential metals exposure and MetS prevalence in a cross-sectional study.

Methods: Concentrations of 8 urinary essential metals and plasma C-reactive protein (CRP) were quantified in 3272 adults from Wuhan-Zhuhai cohort. Urinary essential metals were adjusted by the corresponding urinary creatinine concentrations and reported as  $\mu$ g/mmol creatinine. Multivariable logistic regression and linear regression

In the single-metal models, we observed positive dose-dependent relationships of urinary copper and zinc with MetS prevalence.

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models were used to evaluate dose-response relationships between essential metals, plasma CRP, and MetS prevalence. Mediation analysis was performed to investigate the role of plasma CRP in the associations between urinary essential metals and MetS prevalence.

Results: In the single-metal models, we observed positive dose-dependent relationships of urinary copper and zinc with MetS prevalence. Compared with the lowest quartiles of urinary metals, the ORs (95% CI) of MetS in the highest quartiles were 1.40 (1.03, 1.91) for urinary copper and 2.07 (1.51, 2.84) for zinc, respectively. The dose-dependent relationships of zinc and copper with MetS remained significant in the multiple-metal models and Bayesian kernel machine regression (BKMR) models. No significant associations were observed between others essential metals (e.g. manganese, iron, cobalt, selenium, chromium, molybdenum) and MetS in this general population (all P value > 0.05). In addition, urinary copper and zinc increased monotonically with plasma CRP elevation, and plasma CRP was positively associated with the MetS prevalence. Mediation analysis indicated that plasma CRP mediated 5.2% and 3.2% in the associations of urinary copper and zinc with MetS prevalence, respectively.

Conclusions: Elevated concentrations of urinary copper and zinc were associated with increased prevalence of MetS. Systemic inflammation may play an important role in the associations of copper and zinc exposure with MetS.

Authors: Jixuan Ma, Yun Zhou, Dongming Wang, Yanjun Guo, Bin Wang, Yiju Xu, Weihong Chen

Full Source: Environmental international. 2020 Jul;140:105802. doi: 10.1016/j.envint.2020.105802. Epub 2020 May 28.

NHL and other specified LN were increased in exposed vs unexposed workers.

## OCCUPATIONAL

### Benzene exposure-response and risk of lymphoid neoplasms in Chinese workers: A multicenter case-cohort study

2020-05-31

Background: While international agreement supports a causal relationship of benzene exposure with acute myeloid leukemia, there is debate about benzene and lymphoid neoplasm risks.

Methods: In a case-cohort study with follow-up of 110 631 Chinese workers during 1972-1999, we evaluated benzene exposure-response for non-Hodgkin lymphoma (NHL), lymphoid leukemias (LL), acute lymphocytic leukemia (ALL), and total lymphoid neoplasms (LN). We

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estimated benzene exposures using state-of-the-art hierarchical modeling of occupational factors calibrated with historical routine measurements and evaluated cumulative exposure-response using Cox regression. Results: NHL and other specified LN were increased in exposed vs unexposed workers. However, there was no evidence of exposure-response for NHL or other specified LN. Based on a linear exposure-response, relative risks at 100 parts per million-years (RR at 100 ppm-years) for cumulative benzene exposure using a 2-year lag (exposure at least 2 years before the time at risk) were 1.05 for NHL (95 percent confidence interval (CI) = 0.97, 1.27; 32 cases), 1.11 for LL (95% CI < 0, 1.66; 12 cases), 1.21 for ALL (95% CI < 0, 3.53; 10 cases), and 1.02 for total LN (95% CI < 0, 1.16; 49 cases). No statistically significant exposure-response trends were apparent for these LN for 2 to <10-year or ≥10-year lags. NHL risks were not significantly modified by sex, age, or year at first exposure, attained age, or time since exposure.

Conclusion: Given the study strengths and limitations, we found little evidence of exposure-response for benzene and NHL, LL, ALL, or total LN, although NHL and other specified LN were increased in exposed vs unexposed individuals.

Authors: Martha S Linet, Ethel S Gilbert, Rudolf Vermeulen, Graça M Soares, Song-Nian Yin, Lutzen Portengen, Richard B Hayes, Bu-Tian Ji, Qing Lan, Gui-Lan Li, Nathaniel Rothman  
Full Source: American Journal of Industrial Medicine. 2020 May 31. doi: 10.1002/ajim.23142. Online ahead of print.

### Hexavalent chromium induces mitochondrial dynamics disorder in rat liver by inhibiting AMPK/PGC-1α signaling pathway

2020-05-23

Occupational exposure to hexavalent chromium (Cr(VI)) can cause cytotoxicity and carcinogenicity. In this study, we established a liver injury model in rats via intraperitoneal injection of potassium dichromate (0, 2, 4, and 6 mg/kg body weight) for 35 d to investigate the mechanism of Cr(VI)-induced liver injury. We found that Cr(VI) induced hepatic histopathological lesions, oxidative stress, and apoptosis and reduced the expression of mitochondrial-related regulatory factors such as adenosine 5'-monophosphate-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α) in a dose-dependent manner. Furthermore, Cr(VI) promoted mitochondrial division and inhibited fusion, leading to increased expression of caspase-3 and production of mitochondrial reactive oxygen species. Our study

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demonstrates that long-term exposure to Cr(VI) induces mitochondrial dynamics disorder by inhibiting AMPK/PGC-1α signaling pathway in rat liver.

Authors: Qingyue Yang, Bing Han, Jiangdong Xue, Yueying Xue, Siyu Li, Yan Liu, Pengfei Wu, Xiaoqiao Wang, Zhigang Zhang  
Full Source: Environmental Pollution (Barking, Essex: 1987). 2020 May 23;265(Pt A):114855. doi: 10.1016/j.envpol.2020.114855. Online ahead of print.

Furthermore, Cr(VI) promoted mitochondrial division and inhibited fusion, leading to increased expression of caspase-3 and production of mitochondrial reactive oxygen species.