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CHEMICAL EFFECTS

Associations between per- and polyfluoroalkyl substances (PFAS) and diabetes in two population-based cohort studies from Sweden

2023-03-24

Background: Per- and polyfluoroalkyl substances (PFAS) have been suggested to contribute to the development of metabolic diseases such as obesity, diabetes and non-alcoholic fatty liver disease (NAFLD). However, evidence from epidemiological studies remain divergent. The aim of the present study was to evaluate associations between PFAS exposure and prevalent diabetes in a cross-sectional analysis and fasting glucose in a longitudinal analysis.

Methods: In 2373 subjects aged 45-75 years from the EpiHealth study, three PFAS; perfluorohexanesulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) were analyzed in plasma together with information on prevalent diabetes. Participants in the PIVUS study (n = 1016 at baseline, all aged 70 years) were followed over 10 years regarding changes in plasma levels of six PFAS; PFHxS, PFOA, PFOS, perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUnDA), and changes in plasma levels of fasting glucose.

Results: In the EpiHealth study, no overall associations could be observed between the levels of PFOA, PFOS or PFHxS and prevalent diabetes. However, there was a significant sex-interaction for PFOA ($p = 0.02$), and an inverse association could be seen between PFOA (on a SD-scale) and prevalent diabetes in women only (OR: 0.71, 95% CI: 0.52, 0.96, p -value: 0.02). This association showed a non-monotonic dose-response curve. In the PIVUS study, inverse relationships could be observed between the changes in levels (ln-transformed) of PFOA and PFUnDA vs the change in fasting glucose levels (ln-transformed) over 10 years ($p = 0.04$ and $p = 0.02$, respectively). As in EpiHealth, these inverse associations were significant only in women (PFOA: β : -0.03, $p = 0.02$, PFUnDA: β : -0.03, $p = 0.03$).

Impact: Exposure to per- and polyfluoroalkyl substances (PFAS) has been linked to unfavorable human health, including metabolic disorders such as obesity, diabetes and non-alcoholic fatty liver disease. However, results from in vivo, in vitro and epidemiological studies are incoherent. The aim of the present study was therefore to investigate associations between PFAS and diabetes in a cross-sectional study and glucose levels in a longitudinal study. Results show inverse associations in women only.

Background: Per- and polyfluoroalkyl substances (PFAS) have been suggested to contribute to the development of metabolic diseases such as obesity, diabetes and non-alcoholic fatty liver disease (NAFLD).

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Results also display non-monotonic dose response curves (i.e., that only low levels of PFOA are related to higher probability of prevalent diabetes). This suggests that sex differences and complex molecular mechanisms may underlie the observed findings. A better understanding of the factors and molecular mechanisms contributing to such differences is recognized as an important direction for future research.

Conclusions: PFOA was found to be inversely related to both prevalent diabetes and changes in plasma glucose levels among women only. Thus, our findings suggest there are sex differences in the inverse relationship of PFOA and type 2 diabetes and glucose levels.

Authors: Linda Dunder, Samira Salihovic, Sölve Elmståhl, P Monica Lind, Lars Lind

Full Source: Journal of exposure science & environmental epidemiology 2023 Mar 24. doi: 10.1038/s41370-023-00529-x.

Individual and joint effects of phthalates exposure on the risk of early miscarriage

2023-03-23

Background: The exposure levels of phthalates in humans have dropped dramatically. Little is known about the individual and joint effects of phthalates exposure at low levels on the risk of early miscarriage.

Objective: To examine the association between exposure to phthalates individually or as a mixture and early miscarriage.

Methods: A case-control study was conducted in Shanghai, China during 2019-2020. A total of 291 women seeking medical services due to miscarriage (cases) and 308 women planning to terminate an unintended pregnancy (controls) within 12 gestational weeks were recruited. Urinary concentrations of eight phthalate metabolites were determined by ultra-performance liquid chromatography. We included 534 women in the main analysis who had available data on both phthalates exposure and complete information on potential confounders. We used logistic regression and Bayesian kernel machine regression (BKMR) to examine the associations of concentrations of phthalates with miscarriage.

Results: Among the phthalate metabolites, mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) had the highest concentration (8.10 ng/mL), followed by mono(2-ethyl-5-oxohexyl) phthalate (MEOHP, 2.68 ng/mL) and monobutyl phthalate (MBP, 2.24 ng/mL). Higher concentrations of MBP, mono(2-ethylhexyl) phthalate (MEHP), MEHHP, MEOHP and the molar sum of di(2-ethylhexyl) phthalate (DEHP) metabolites (Σ DEHPm) were associated with an increased risk of miscarriage exhibiting a dose-response relationship. The most evident association of miscarriage was

Background: The exposure levels of phthalates in humans have dropped dramatically.

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found with Σ DEHPm, with adjusted odds ratio (95% confidence interval) of 1.94 (1.14, 3.31) for the second quartile, 2.83 (1.67, 4.79) for the third quartile and 4.28 (2.49, 7.37) for the fourth quartile compared to the first quartile. Consistently, the phthalate mixture was positively associated with the risk of miscarriage and DEHP was the predominant contributor to the joint effect in BKMR model.

Impact: Phthalates are a family of synthetic chemicals mainly used as plasticizers, solvents and additives in a large variety of industrial and consumer products, including food packing materials, toys, gloves, medical devices and personal care products. Although exposure levels of phthalates of pregnant women have declined sharply over the past few decades, phthalates exposure was still associated with an increased risk of early miscarriage. Our findings suggest that future researchers and policy makers might need to take low-dose effects of phthalates into account regarding the reproductive toxicity of phthalates exposure in humans.

Significance: Our findings contribute to the awareness of the reproductive toxic potential of phthalates at low levels in humans and support the ongoing efforts to further reduce exposure to phthalates.

Authors: Honglei Ji, Zhiping Wu, Da Chen, Maohua Miao, Hexia Chen, Wen Shuai, Hong Liang, Wei Yuan

Full Source: Journal of exposure science & environmental epidemiology 2023 Mar 23. doi: 10.1038/s41370-023-00533-1.

Joint effects of temperature and copper exposure on developmental and gene-expression responses of the marine copepod *Tigriopus japonicus*

2023-03-24

There is growing contamination of copper (Cu) in the marine environment, particularly after the ban of organotin compounds and the increase of the use of Cu-based antifouling paints. Although there are increasing research interests in temperature-dependent chemical toxicity to aquatic organisms, most existing studies focused on acute impacts of chemicals at high concentrations. This study aimed to investigate the interacting effect of temperature and copper exposure at environmentally relevant concentrations on survival and development in the marine copepod *Tigriopus japonicus* with a partial life-cycle toxicity test. Expressions of five stress response genes in the copepod, namely two glutathione S-transferases (GST-S and GST-O), two heat shock proteins (HSP70 and HSP90), and glutathione reductase (GR) were also investigated. The copepod's survival was significantly impaired at 15 °C after development to adult stage, while its developmental time reduced significantly

There is growing contamination of copper (Cu) in the marine environment, particularly after the ban of organotin compounds and the increase of the use of Cu-based antifouling paints.

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with increasing temperature. Copper at the two environmentally relevant test concentrations had no significant impacts on these apical endpoints whereas the interaction between Cu and temperature was more significant in modulating gene expressions. GST-S, GST-O and HSP90 genes in copepods exposed to 100 μ g Cu L⁻¹ were significantly upregulated at 20 °C. At 32 °C, most genes were either insignificantly expressed or down-regulated, compared to the control, likely suggesting that thermal stress inhibited the copepod's antioxidative defense system. Overall, the results revealed that the joint Cu and thermal stresses have significantly elicited antioxidative system in the copepods. It clearly demonstrated the need for more fundamental studies about potential impacts of different environmental factors such as temperature on chemical toxicity under realistic scenario of marine pollution.

Authors: Adela Jing Li, Racliffe Weng Seng Lai, Guang-Jie Zhou, Priscilla To Yan Leung, Eddy Y Zeng, Kenneth Mei Yee Leung

Full Source: Ecotoxicology (London, England) 2023 Mar 24. doi: 10.1007/s10646-023-02643-w.

ENVIRONMENTAL RESEARCH

Occurrence, source estimation, and risk assessment of Polycyclic Aromatic Hydrocarbons in coastal seawaters from the Quintero Industrial Complex (Valparaíso, Chile)

2023-03-21

In the 1960s, the Quintero industrial complex was inaugurated in Chile. This began a history of dramatic anthropogenic impacts on the Chilean coast. Among the known, we could mention high atmospheric emissions of chemicals due to combustion processes and frequent oil spills. For this reason, we surveyed the concentrations of fifteen EPAPAHs in the surface coastal waters of the Quintero Bay area in 2015. The levels found are in the range of the highest levels when reviewing the literature (0.97 μ g L⁻¹ up to 9.84 μ g L⁻¹). The highest levels were found in the vicinity of the industrial complex and decreased in the other two zones. The concentration of individual compounds significantly exceeds the levels recommended by the EPA (Environmental Protection Agency) and the EU water framework directive (WFD). The risk estimations revealed that PAH concentrations represent high-risk for wildlife. Molecular ratios of PAHs were used to identify the possible sources, being these were mainly of pyrogenic origin, agreeing with an origin in the combustion of wood, coal, grass, and fossil

In the 1960s, the Quintero industrial complex was inaugurated in Chile.

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fuels. This study contributes to the first data for surface water in a country's highly impacted industrial coastal area.

Authors: C J Galbán-Malagón, J Zapata, D J Perez-Venegas, R Vargas, N Latorre-Padilla, T Luarte, C Ahrendt, A Hirmas-Olivares, V Gómez-Aburto, P Tapia, V Isamit, P Arce, C Sánchez, K Pozo
Full Source: The Science of the total environment 2023 Mar 21;162957. doi: 10.1016/j.scitotenv.2023.162957.

Using blood lead concentrations of wildlife sentinels to identify environmental risk factors of lead exposure for public health and wildlife rehabilitation efforts

2023-03-24

Lead poisoning remains a persistent health issue for both humans and wildlife, despite strides to reduce lead contamination in the environment. Using Geographic Information Systems (GIS), this study explores the associations between blood lead levels (BLLs) in wildlife sentinels and possible built environment lead exposure risk factors in the Minneapolis-Saint Paul, Minnesota urban area. Results show a high-level of heterogeneity in animal BLLs (n = 472) across our urban environment and suggest that each kilometer increase in road density is associated with a 17.07% (95% CI: 1.48%, 35.05%) increase in BLL in our study species of Virginia opossums and Eastern gray squirrels, and a 14.28% (95% CI: 1.16%, 29.09%) increase in BLL of rock pigeons. For squirrels and opossums, we see an additional 5.72% (95% CI: 0.59%, 10.85%) increased risk of BLL for every 1000 people per square-mile. The relationship between animal sentinels and environmental hazards can give us an insight into the potential lead exposure risks for humans. The use of wildlife sentinel data to explore environmental risk factors supports a One Health approach to better address public health questions and aid in wildlife rehabilitation related to residual lead poisoning from ambient environmental exposures.
Authors: Mito Imagawa, Marcus Rushing, Allison Carter, Renee Schott, Jesse D Berman
Full Source: Ecotoxicology (London, England) 2023 Mar 24. doi: 10.1007/s10646-023-02642-x.

Air pollution and stroke hospitalization in the Beibu Gulf Region of China: A case-crossover analysis

2023-03-23

Background: The relationship between air pollution and stroke has been extensively studied, however, the evidence regarding the association

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between air pollution and hospitalization due to stroke and its subtypes in coastal areas of China is limited.

Objective: To estimate the associations between air pollution and hospitalizations of stroke and its subtypes in the Beibu Gulf Region of China.

Methods: We conducted a time-stratified case-crossover study in 15 cities in Beibu Gulf Region in China from 2013 to 2016. Exposures to PM1, PM2.5, PM10, SO2, NO2, O3, and CO on the case and control days were assessed at residential addresses using bilinear interpolation. Conditional logistic regressions were constructed to estimate city-specific associations adjusting for meteorological factors and public holidays. Meta-analysis was further conducted to pool all city-level estimates.

Results: There were 271,394 case days and 922,305 control days. The odds ratios (ORs) for stroke hospitalizations associated with each interquartile range (IQR) increase in 2-day averages of SO2 (IQR: 10.8 µg/m³), NO2 (IQR: 11.2 µg/m³), and PM10 (IQR: 37 µg/m³) were 1.047 (95% CI [confidence interval]: 1.015-1.080), 1.040 (95% CI: 1.027-1.053), and 1.018 (95% CI: 1.004-1.033), respectively. The associations with hospitalizations of ischemic stroke were significant for all seven pollutants, while the association with hemorrhagic stroke was significant only for CO. The associations of SO2, NO2, and O3 with stroke hospitalization were significantly stronger in the cool season.
Conclusions: Short-term increase in SO2, NO2, and PM10 might be important triggers of stroke hospitalization. All seven air pollutants were associated with ischemic stroke hospitalization, while only CO was associated with hemorrhagic stroke hospitalization. These results should be considered in public health policy.

Authors: Meijun Li, Randall C Edgell, Jing Wei, Haopeng Li, Zhengmin Min Qian, Jin Feng, Fei Tian, Xiaojie Wang, Qinghua Xin, Miao Cai, Hualiang Lin
Full Source: Ecotoxicology and environmental safety 2023 Mar 23;255:114814. doi: 10.1016/j.ecoenv.2023.114814.

The relationship between air pollution and stroke has been extensively studied.

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PHARMACEUTICAL/TOXICOLOGY

Prediction of in vivo prenatal chlorpyrifos exposure leading to developmental neurotoxicity in humans based on in vitro toxicity data by quantitative in vitro-in vivo extrapolation

2023-03-07

Introduction: Epidemiological studies in children suggested that in utero exposure to chlorpyrifos (CPF), an organophosphate insecticide, may cause developmental neurotoxicity (DNT). We applied quantitative in vitro-in vivo extrapolation (QIVIVE) based on in vitro concentration and non-choline esterase-dependent effects data combined with Benchmark dose (BMD) modelling to predict oral maternal CPF exposure during pregnancy leading to fetal brain effect concentration. By comparing the results with data from epidemiological studies, we evaluated the contribution of the in vitro endpoints to the mode of action (MoA) for CPF-induced DNT. Methods: A maternal-fetal PBK model built in PK-Sim® was used to perform QIVIVE predicting CPF concentrations in a pregnant women population at 15 weeks of gestation from cell lysate concentrations obtained in human induced pluripotent stem cell-derived neural stem cells undergoing differentiation towards neurons and glia exposed to CPF for 14 days. The in vitro concentration and effect data were used to perform BMD modelling. Results: The upper BMD was converted into maternal doses which ranged from 3.21 to 271 mg/kg bw/day. Maternal CPF blood levels from epidemiological studies reporting DNT findings in their children were used to estimate oral CPF exposure during pregnancy using the PBK model. It ranged from 0.11 to 140 µg/kg bw/day. Discussion: The effective daily intake doses predicted from the in vitro model were several orders of magnitude higher than exposures estimated from epidemiological studies to induce developmental non-cholinergic neurotoxic responses, which were captured by the analyzed in vitro test battery. These were also higher than the in vivo LOEC for cholinergic effects. Therefore, the quantitative predictive value of the investigated non-choline esterase-dependent effects, although possibly relevant for

Introduction: Epidemiological studies in children suggested that in utero exposure to chlorpyrifos (CPF), an organophosphate insecticide, may cause developmental neurotoxicity (DNT).

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other chemicals, may not adequately represent potential key events in the MoA for CPF-associated DNT.

Authors: Engi Abdelhady Algharably, Emma Di Consiglio, Emanuela Testai, Francesca Pistollato, Anna Bal-Price, Abdulkarim Najjar, Reinhold Kreutz, Ursula Gundert-Remy
Full Source: *Frontiers in pharmacology* 2023 Mar 7;14:1136174. doi: 10.3389/fphar.2023.1136174.

Occurrence of legacy and alternative per- and polyfluoroalkyl substances in serum from high exposure population and their disrupting effects on serum lipids and thyroid function

2023-03-21

High exposure of per- and polyfluoroalkyl substances (PFAS) has been reported in main chemical production areas in China, while epidemiological study on exposure risk of PFAS is still limited. In this study, legacy and alternative PFAS were measured in serum samples from 161 adults living in Laizhou Bay, a famous chemical production area located in Shandong province, Northern China. Based on the concentrations of serum PFAS, the disrupting effects of PFAS on serum lipids and thyroid function were further explored. The results showed that the serum perfluorooctanoic acid (PFOA) (geometric mean (GM): 60 ng/mL) in this region was even higher than serum PFOA of residents living in PFOA contaminated water districts in United States and Sweden. 100 % of the serum PFOA was higher than the reference dose for increased total cholesterol (TC). Consistently, higher serum PFOA was marginally correlated with increased TC level ($p = 0.062$) and low-density lipoprotein ($p = 0.065$). In addition, higher perfluoroisopropyl perfluorooctanesulfonate and 6:2 chlorinated polyfluoroalkyl ether sulfonates (6,2 Cl-PFESA) were significantly correlated with increased high-density lipoprotein ($p = 0.040, 0.022$). No significant association was observed between individual PFAS and any thyroid function biomarker. However, using the principal component analysis derived factors to represent the co-exposure patterns, co-exposure of legacy long-chain PFAS showed synergistic effects on the free thyroxine, while the mixture of alternative PFAS showed a synergistic influence on the total and free triiodothyronine.

Authors: Jiaying Liu, Linlin Song, Jing Zhan, Yunxin Zhong, Zhixiong Shi
Full Source: *The Science of the total environment* 2023 Mar 21;162988. doi: 10.1016/j.scitotenv.2023.162988.

High exposure of per- and polyfluoroalkyl substances (PFAS) has been reported in main chemical production areas in China, while epidemiological study on exposure risk of PFAS is still limited.

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OCCUPATIONAL

Assessment of occupational health risk due to inhalation of chemical compounds in an aircraft maintenance, repair, and overhaul company

2023-03-25

This study was conducted in an aircraft maintenance, repair, and overhaul (MRO) company in 2021 to identify the extent of occupational exposures and quantitative assessment of the health risk due to inhalation of chemical compounds. According to the inspection of different parts of this company, heavy metals including Co, Cd, Ni, Pb, Cr(VI), and Mn and organic compounds including benzene, toluene, ethylbenzene, xylene (BTEX), and methyl ethyl ketone (MEK) were selected for health risk assessment. In total, the air in the inhalation area of active workers was sampled in 51 workstations. Measurement of the above pollutants showed that the average occupational exposure to Cd, Pb, and all organic compounds fell within the acceptable range of occupational exposure standard, while the measured values for Co, Ni, Mn, and Cr(VI) exceeded the standard limit. According to calculations, the highest carcinogenic risk (CR) was seen in the plating (airplane) workshop for exposure to Cr(VI) ($7.58E-01$), and the lowest CR was observed in the electronic workshop for exposure to Pb ($7.75E-08$). The highest non-carcinogenic hazard (HQ) was found in the welding workshop for exposure to Co ($1.00E+04$), while the lowest HQ was related to toluene in the fabrication workshop ($9.10E-03$). Considering the high rate of exposure indicators, CR and HQ exceeded the standards set by the American Environmental Protection Agency (EPA) in most workshops. Accordingly, company managers should take the necessary measures to reduce the vulnerability of individuals working in areas with unacceptable CR and HQ.

Authors: Mohammadmahdi Khalili, Touraj Nasrabadi

Full Source: Environmental science and pollution research international 2023 Mar 25. doi: 10.1007/s11356-023-26572-7.

This study was conducted in an aircraft maintenance, repair, and overhaul (MRO) company in 2021 to identify the extent of occupational exposures and quantitative assessment of the health risk due to inhalation of chemical compounds.

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Characterization of welding fume and airborne heavy metals in electronic manufacturing workshops in Hangzhou, China: implication for occupational population exposure

2023-03-25

Occupational exposure to contaminants created by electronic manufacturing process is not well characterized. The aim of this study was to carry out risk assessments of exposure to welding fume and airborne heavy metals (HMs) in electronic manufacturing workshops. Seventy-six air samples were collected from five sites in Hangzhou, China. In welding workshops, the most abundant contaminant found was welding fume, followed by Fe, Mn, Zn, Cu, Pb, Cd, and Cr. The concentration of Mn was positively correlated with Fe ($r = 0.906$). When compared with non-welding workshops, the Fe content in the air of welding workshops increased significantly ($P < 0.05$), while the Cu content decreased significantly ($P < 0.05$). Singapore semi-quantitative health risk assessment model and the United States Environmental Protection Agency (US EPA) inhalation risk assessment model were applied to assess the occupational exposure. In welding workshops, the levels of 8-h time weighted average (8 h-TWA) calculated for welding fume (range $0.288 \sim 6.281$ mg/m³), Mn (range $Nd \sim 0.829$ mg/m³), and Fe (range $0.027 \sim 2.234$ mg/m³) partly exceeded the permissible limits. While, in non-welding workshops, the average of 8 h-TWA for Cu (0.411 mg/m³) was higher than the limit. The risk rates (RR) assessed for Pb (2.4 vs 1.7), Mn (2.0 vs 1.4), and Fe (1.4 vs 1.0) were higher in welding workshops than that in non-welding workshops, but Cu (1.0 vs 2.2) were lower. The mean excess lifetime cancer risks (ELCR) in welding ($5.59E-06$ per 1000 people) and non-welding ($1.88E-06$ per 1000 people) workshops were acceptable. The mean non-cancer risk (HQ) estimated for Mn was greater than 10 in both welding (HQ = 164) and non-welding (HQ = 11.1) workshops. These results indicate that there was a risk of occupational exposure implication in the electronic manufacturing workshops. Reducing contaminant exposure through engineering controls and management strategies, such as efficient ventilation and reducing exposure hours, is thus suggested.

Authors: Ling Zhang, Jia-Mian Yu, Xiao-Yue Shan, Ji Shao, Hai-Peng Ye

Full Source: Environmental science and pollution research international 2023 Mar 25. doi: 10.1007/s11356-023-26569-2.

Occupational exposure to contaminants created by electronic manufacturing process is not well characterized.