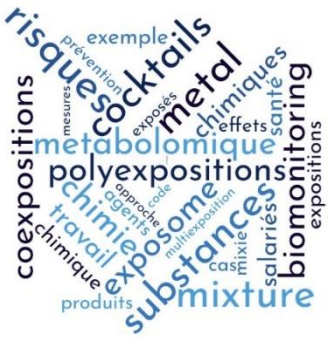

Bulletin de veille
Polyexpositions chimie-chimie
N°4 – juin, juillet 2024

Objectif : la polyexposition agent chimique/chimie est un sujet de plus en plus préconisé pour étudier l'évaluation du risque professionnel et sa prévention. L'objectif est de connaitre les travaux récents qui sont publiés sur le sujet et identifier des moyens d'analyse, et d'interprétation de la multi-exposition à plusieurs composés chimiques. Ce bulletin a été réalisé à partir d'une surveillance de littérature récente sur les bases internationales Web of Sciences, la base HAL Thèses et la base documentaire INRS-Biblio.

La validation des informations fournies (exactitude, fiabilité, pertinence par rapport aux principes de prévention, etc.) est du ressort des auteurs des articles signalés dans la veille. Les informations ne sont pas le reflet de la position de l'INRS. Les éléments issus de cette veille sont fournis sans garantie d'exhaustivité. Les liens mentionnés dans le bulletin donnent accès aux documents sous réserve d'un abonnement à la ressource.

Actualités web sélectionnées

- Consulté le 19 juin. L'Anses et l'OFB signent un partenariat au service de la santé du vivant et des milieux (www.anses.fr) L'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (Anses) et l'Office français de la biodiversité (OFB) engagent un partenariat pour renforcer leurs collaborations et partager leurs compétences respectives sur la santé humaine, la santé animale la santé des écosystèmes, dans une approche « One Health – une seule santé » et dans le contexte du changement climatique.

- Symposium sur la recherche en exposome le 25/09/2024 : Barcelona Exposome Symposium 2024 - ISGLOBAL " Cet événement vise à faciliter le partage des connaissances, des idées et des ressources au sein de la communauté de recherche sur l'exposome dans la région de Barcelone.

- Publié le 14 juin 2024. Le centre HERCULES de l'université Emory, financé par le NIEHS, a fait l'objet d'un article de couverture dans le magazine Rollins pour son rôle dans l'avancement de la recherche

sur l'exposome. National Institute of Environmental Health Sciences: HERCULES Center Members: Exposing the Exposome (nih.gov)

- Publié le 2 juillet 2024. Interview d'expert - Exposition de la population aux pesticides, résultat de l'étude Esteban 2014-2016 (santepubliquefrance.fr)

- Publié le 6 juillet 2024. Une équipe de l'université d'Amsterdam préconise dans un article en open access (Journal of the American Chemical Society), l'utilisation de l'apprentissage automatique de l'IA, en complément des stratégies existantes de détection et d'identification de toutes les molécules auxquelles nous sommes exposés. University of Amsterdam: Harnessing Machine Learning and AI to Comprehend the Full Scope of Chemicals Around Us – India Education

- Publié le 9 juillet 2024. « Quid des facteurs environnementaux sur le développement et la santé mentale de l'enfant ? » Parmi les cinq projets retenus par le Health data Club lors de son appel à projets dédié à la recherche et l'innovation en santé-environnement, la recherche CHILD-Environment & Development s'intéresse à l'impact de l'exposome sur le développement psychomoteur et la santé mentale de l'enfant. https://www.santementale.fr/2024/07/quid-facteurs-environnementaux-sur-developpement-enfant/

- Colloque de l'IRSST 2024 (irsst.qc.ca) le 28 novembre prochain sur **les risques générés par les activités de collecte et de tri des matières résiduelles** : santé et sécurité au cœur de la gestion des matières résiduelles. Défis, perspectives, et pratiques.

Sommaire

Reviews

Rafeletou, A., Niemi, J. V. L., Lagunas-Rangel, F. A., Liu, W., Kudlak, B., Schioth, H. B.
The exposure to UV filters: Prevalence, effects, possible molecular mechanisms of action and interactions within mixtures.
Science of the Total Environment 2024; Vol. 928

Substances that can absorb sunlight and harmful UV radiation such as organic UV filters are widely used in cosmetics and other personal care products. Since humans use a wide variety of chemicals for multiple purposes it is common for UV filters to co-occur with other substances either in human originating specimens or in the environment. There is increasing interest in understanding such co-occurrence in form of potential synergy, antagonist, or additive effects of biological systems. This review focuses on the collection of data about the simultaneous occurrence of UV filters oxybenzone (OXYB), ethylexyl-methoxycinnamate (EMC) and 4-methylbenzylidene camphor (4-MBC) as well as other classes of chemicals (such as pesticides, bisphenols, and parabens) to understand better any such interactions considering synergy, additive effect and antagonism. Our analysis identified >20 different confirmed synergies in 11 papers involving 16 compounds. We also highlight pathways (such as transcriptional activation of estrogen receptor, promotion of estradiol synthesis, hypothalamic-pituitary-gonadal (HPG) axis, and upregulation of thyroid-hormone synthesis) and proteins (such as Membrane Associated Progesterone Receptor (MAPR), cytochrome P450, and heat shock protein 70 (Hsp70)) that can act as important key nodes for such potential interactions. This article aims to provide insight into the molecular mechanisms on how commonly used UV filters act and may interact with other chemicals.

https://doi.org/10.1016/j.scitotenv.2024.170999

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Purcaro, C., Marramiero, L., Santangelo, C., Bondi, D., Di Filippo, E. S.
Exposome on skeletal muscle system: a mini-review.
European Journal of Applied Physiology 2024

Exposomics is an ever-expanding field which captures the cumulative exposures to chemical, biological, physical, lifestyle, and social factors associated with biological responses. Since skeletal muscle is currently considered as the largest secretory organ and shows substantial plasticity over the life course, this reviews addresses the topic of exposome and skeletal muscle by reviewing the state-of-the-art evidence and the most intriguing perspectives. Muscle stem cells react to stressors via phosphorylated eukaryotic initiation factor 2 alpha and tuberous sclerosis 1, and are sensible to hormetic factors via sirtuin 1. Microplastics can delay muscle regeneration via p38 mitogen-activated protein kinases and induce transdifferentiation to adipocytes via nuclear factor kappa B. Acrolein can inhibit myogenic differentiation and disrupt redox system. Heavy metals have been associated with reduced muscle strength in children. The deep study of pollutants and biological features can shed new light on neuromuscular pathophysiology. The analysis of a time-varying and dynamic exposome risk score from a panel of exposure and phenotypes of interest is promising. The systematization of hormetic factors and the role of the microbiota in modulating the effects of exposure on skeletal muscle responses are also promising. The comprehensive exposure assessment and its interactions with endogenous processes and the resulting biological effects deserve more efforts in the field of muscle health across the lifespan.

https://doi.org/10.1007/s00421-024-05515-1

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Nobile, F., Dimakopoulou, K., Astrom, C., Coloma, F., Dadvand, P., De Bont, J.*, et al.*
External exposome and all-cause mortality in European cohorts: the EXPANSE project.
Frontiers in epidemiology 2024; Vol. 4 p 1327218.

Background: Many studies reported associations between long-term exposure to environmental factors and mortality; however, little is known on the combined effects of these factors and health. We aimed to evaluate the association between external exposome and all-cause mortality in large administrative and traditional adult cohorts in Europe.
Methods: Data from six administrative cohorts (Catalonia, Greece, Rome, Sweden, Switzerland and the Netherlands, totaling 27,913,545 subjects) and three traditional adult cohorts (CEANS-Sweden, EPIC-NL-the Netherlands, KORA-Germany, totaling 57,653 participants) were included. Multiple exposures were assigned at the residential addresses, and were divided into three a priori defined domains: (1) air pollution [fine particulate matter (PM2.5), nitrogen dioxide (NO_2), black carbon (BC) and warm-season Ozone (warm-O3)]; (2) land/built environment (Normalized Difference Vegetation Index-NDVI, impervious surfaces, and distance to water); (3) air temperature (cold- and warm-season mean and standard deviation). Each domain was synthesized through Principal Component Analysis (PCA), with the aim of explaining at least 80% of its variability. Cox proportional-hazards regression models were applied and the total risk of the external exposome was estimated through the Cumulative Risk Index (CRI). The estimates were adjusted for individual- and area-level covariates.
Results: More than 205 million person-years at risk and more than 3.2 million deaths were analyzed. In single-component models, IQR increases of the first principal component of the air pollution domain were associated with higher mortality [HRs ranging from 1.011 (95% CI: 1.005-1.018) for the Rome cohort to 1.076 (1.071-1.081) for the Swedish cohort]. In contrast, lower levels of the first principal component of the land/built environment domain, pointing to reduced vegetation and higher percentage of impervious surfaces, were associated with higher risks. Finally, the CRI of external exposome increased mortality for almost all cohorts. The associations found in the traditional adult cohorts were generally consistent with the results from the administrative ones, albeit without reaching statistical significance.
Discussion: Various components of the external exposome, analyzed individually or in combination, were associated with increased mortality across European cohorts. This sets the stage for future research on the connections between various exposure patterns and human health, aiding in the planning of healthier cities.

https://doi.org/10.3389/fepid.2024.1327218

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Peters, S., Undem, K., Solovieva, S., Selander, J., Schlunssen, V., Oude Hengel, K. M.*, et al.*
Narrative review of occupational exposures and noncommunicable diseases.
Annals of work exposures and health 2024; Vol. 68 (6) p 562-580.

OBJECTIVE: Within the scope of the Exposome Project for Health and Occupational Research on applying the exposome concept to working life health, we aimed to provide a broad overview of the status of knowledge on occupational exposures and associated health effects across multiple noncommunicable diseases (NCDs) to help inform research priorities.
METHODS: We conducted a narrative review of occupational risk factors that can be considered to have "consistent evidence for an association," or where there is "limited/inadequate evidence for an association" for 6 NCD groups: nonmalignant respiratory diseases; neurodegenerative diseases; cardiovascular/metabolic diseases; mental disorders; musculoskeletal diseases; and cancer. The assessment was done in expert sessions, primarily based on systematic reviews, supplemented with narrative reviews, reports, and original studies. Subsequently, knowledge gaps were identified, e.g.

based on missing information on exposure-response relationships, gender differences, critical time-windows, interactions, and inadequate study quality.
RESULTS: We identified over 200 occupational exposures with consistent or limited/inadequate evidence for associations with one or more of 60+ NCDs. Various exposures were identified as possible risk factors for multiple outcomes. Examples are diesel engine exhaust and cadmium, with consistent evidence for lung cancer, but limited/inadequate evidence for other cancer sites, respiratory, neurodegenerative, and cardiovascular diseases. Other examples are physically heavy work, shift work, and decision latitude/job control. For associations with limited/inadequate evidence, new studies are needed to confirm the association. For risk factors with consistent evidence, improvements in study design, exposure assessment, and case definition could lead to a better understanding of the association and help inform health-based threshold levels.
CONCLUSIONS: By providing an overview of knowledge gaps in the associations between occupational exposures and their health effects, our narrative review will help setting priorities in occupational health research. Future epidemiological studies should prioritize to include large sample sizes, assess exposures prior to disease onset, and quantify exposures. Potential sources of biases and confounding need to be identified and accounted for in both original studies and systematic reviews.

https://doi.org/10.1093/annweh/wxae045

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Approche exposome et métabolomique

Shi, C., Yang, J., You, Z., Zhang, Z., Fang, M.
Suspect screening analysis by tandem mass spectra from metabolomics to exposomics.
Trac-Trends in Analytical Chemistry 2024; Vol. 175

Compared to metabolomics, exposomics imposes more stringent requirements for analytical methods, owing to the trace concentrations of exposure chemicals and their complex biotransformation processes. A promising strategy to overcome the challenges in exposomic analysis is suspect screening analysis (SSA). This approach enhances the selectivity, efficiency, and accuracy of analysis by identifying specific parent-product pairs using tandem mass spectrometry (MS/MS). Based on the spectrum information employed in SSA, we have classified the current methods into four primary categories in this review. These include spectral database-based screening, substructure-guided screening, experimental spectrum-based screening, and derivatization-assisted screening. These strategies have evolved into the multiple reaction monitoring (MRM) method through the selection of characteristic fragment ions, optimization of collision energy (CE) and determination of retention time (RT). Furthermore, we evaluated their scope of application and highlighted that advancements in spectral prediction, the acquisition of high-quality MS/MS data, and the computational establishment of robust MS/MS features for SSA.

https://doi.org/10.1016/j.trac.2024.117699

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Song, Y., Qi, Z., Cai, Z.
Application of multiomics mass spectrometry in the research of chemical exposome.
Chinese Journal of Chromatography 2024; Vol. 42 (2), p 120-130.

Environmental factors, such as environmental pollutants, behaviors, and lifestyles, are the leading

causes of chronic noncommunicable diseases. Estimates indicate that approximately 50% of all deaths worldwide can be attributed to environmental factors. The exposome is defined as the totality of human environmental (i.e., all nongenetic) exposures from conception, including general external exposure (e. g., climate, education, and urban environment), specific external exposure (e. g., pollution, physical activity, and diet), and internal exposure (e. g., metabolic factors, oxidative stress, inflammation, and protein modification). As a new paradigm, this concept aims to comprehensively understand the link between human health and environmental factors. Therefore, a comprehensive measurement of the exposome, including accurate and reliable measurements of exposure to the external environment and a wide range of biological responses to the internal environment, is of great significance. The measurement of the general external exposome depends on advances in environmental sensors, personalsensing technologies, and geographical information systems. The determination of exogenous chemicals to which individuals are exposed and endogenous chemicals that are produced or modified by external stressors relies on improvements in methodology and the development of instrumental approaches, including colorimetric, chromatographic, spectral, and mass-spectrometric methods.
This article reviews the research strategies for chemical exposomes and summarizes existing exposome-measurement methods, focusing on mass spectrometry (MS)-based methods. The top-down and bottom-up approaches are commonly used in exposome studies. The bottom-up approach focuses on the identification of chemicals in the external environment (e. g., soil, water, diet, and air), whereas the top-down approach focuses on the evaluation of endogenous chemicals and biological processes in biological samples (e. g., blood, urine, and serum). Low and high resolution MS (LRMS and HRMS, respectively) have become the most popular methods for the direct measurement of exogenous and endogenous chemicals owing to their superior sensitivity, specificity, and dynamic range. LRMS has been widely applied in the targeted analysis of expected chemicals, whereas HRMS is a promising technique for the suspect and unknown screening of unexpected chemicals. The development of MS-based multiomics, including proteomics, metabolomics, epigenomics, and spatial omics, provides new opportunities to understand the effects of environmental exposure on human health. Metabolomics involves the sum of all low molecular-weight metabolites in a living system. Nontargeted metabolomics can measure both endogenous and exogenous chemicals, which would directly link exposure to biological effects, internal dose, and disease pathobiology, whereas proteomics could play an important role in predicting potential adverse health outcomes and uncovering molecular mechanisms. MS imaging (MSI) is an emerging technique that provides unlabeled in-depth measurements of endogenous and exogenous molecules directly from tissue and cell sections without changing their spatial information. MSI.based spatial omics, which has been widely applied in biomarker discovery for clinical diagnosis, as well as drug and pollutant monitoring, is expected to become an effective method for exposome measurement. Integrating these response measurements from metabolomics, proteomics, spatial omics, and epigenomics will enable the generation of new hypotheses to discover the etiology of diseases caused by chemical exposure. Finally, we highlight the major challenges in achieving chemical exposome measurements.

https://doi.org/10.3724/sp.J.1123.2023.10001

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Khoo, S. C., Zhang, N., Luang-In, V., Goh, M. S., Sonne, C., Ma, N. L.
Exploring environmental exposomes and the gut-brain nexus: Unveiling the impact of pesticide exposure.
Environmental Research, 1 June 2024, Vol. 250, 118441.

This review delves into the escalating concern of environmental pollutants and their profound impact on human health in the context of the modern surge in global diseases. The utilisation of chemicals in food production, which results in residues in food, has emerged as a major concern nowadays. By exploring the intricate relationship between environmental pollutants and gut microbiota, the study

reveals a dynamic bidirectional interplay, as modifying microbiota profile influences metabolic pathways and subsequent brain functions. This review will first provide an overview of potential exposomes and their effect to gut health. This paper is then emphasis the connection of gut brain function by analysing microbiome markers with neurotoxicity responses. We then take pesticide as example of exposome to elucidate their influence to biomarkers biosynthesis pathways and subsequent brain functions. The interconnection between neuroendocrine and neuromodulators elements and the gut-brain axis emerges as a pivotal factor in regulating mental health and brain development. Thus, manipulation of gut microbiota function at the onset of stress may offer a potential avenue for the prevention and treatment for mental disorder and other neurodegenerative illness.

https://doi.org/10.1016/j.envres.2024.118441

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Rushing, B. R., Thessen, A. E., Soliman, G. A., Ramesh, A., Sumner, S. C.
The Exposome and Nutritional Pharmacology and Toxicology: A New Application for Metabolomics.
Exposome 2023; Vol. 3 (1) osad008.

The exposome refers to all of the internal and external life-long exposures that an individual experiences. These exposures, either acute or chronic, are associated with changes in metabolism that will positively or negatively influence the health and well-being of individuals. Nutrients and other dietary compounds modulate similar biochemical processes and have the potential in some cases to counteract the negative effects of exposures or enhance their beneficial effects.
We present herein the concept of Nutritional Pharmacology/Toxicology which uses high-information metabolomics workflows to identify metabolic targets associated with exposures. Using this information, nutritional interventions can be designed toward those targets to mitigate adverse effects or enhance positive effects. We also discuss the potential for this approach in precision nutrition where nutrients/diet can be used to target gene-environment interactions and other subpopulation characteristics. Deriving these "nutrient cocktails" presents an opportunity to modify the effects of exposures for more beneficial outcomes in public health.

https://doi.org/10.1093/exposome/osad008

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Cheng, S. L., Hedges, M., Keski-Rahkonen, P., Chatziioannou, A. C., Scalbert, A., Chung, K. F.*, et al.*
Multiomic Signatures of Traffic-Related Air Pollution in London Reveal Potential Short-Term Perturbations in Gut Microbiome-Related Pathways.
Environmental science & technology 2024; Vol. 58 (20) p 8771-8782.

This randomized crossover study investigated the metabolic and mRNA alterations associated with exposure to high and low traffic-related air pollution (TRAP) in 50 participants who were either healthy or were diagnosed with chronic pulmonary obstructive disease (COPD) or ischemic heart disease (IHD). For the first time, this study combined transcriptomics and serum metabolomics measured in the same participants over multiple time points (2 h before, and 2 and 24 h after exposure) and over two contrasted exposure regimes to identify potential multiomic modifications linked to TRAP exposure. With a multivariate normal model, we identified 78 metabolic features and 53 mRNA features associated with at least one TRAP exposure. Nitrogen dioxide (NO2) emerged as the dominant pollutant, with 67 unique associated metabolomic features. Pathway analysis and annotation of metabolic features consistently indicated perturbations in the tryptophan metabolism associated with NO2 exposure, particularly in the gut-microbiome-associated indole pathway. Conditional multiomics networks revealed complex and intricate mechanisms associated with TRAP exposure, with some

effects persisting 24 h after exposure. Our findings indicate that exposure to TRAP can alter important physiological mechanisms even after a short-term exposure of a 2 h walk. We describe for the first time a potential link between NO2 exposure and perturbation of the microbiome-related pathways.

https://doi.org/10.1021/acs.est.3c09148

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Biomonitoring, outils, modèles mathématiques

Wu, L., Zhang, S., Zhang, J., Xin, Y., Niu, P., Li, J.
Associations of heavy metal mixtures with blood pressure among US adults in NHANES 2017-2018 by four statistical models.
Chinese Medical Journal 2024; Vol. 137 (5), p 628-630.

To the Editor: Hypertension is one of the leading risk factors for cardiovascular disease and affects approximately 30% of the adult population. Environmental heavy metal pollution is an important public health concern. Toxic metals may increase the risk of hypertension or other cardiovascular diseases, even beyond the influence of conventional behavioral risk factors. Meanwhile certain essential trace elements, such as selenium, zinc, and iron, are involved in various enzyme reactions directly related to blood pressure regulation and are beneficial to the human body within a specific range. The analysis of health outcomes specific to metal mixtures is challenging by nonlinear relationships and interactions between toxic metals and essential trace elements. The development of innovative statistical methods for analyzing mixtures has greatly facilitated the exploration of the health effects of multiple pollutant exposures, such as Bayesian kernel machine regression (BKMR) and quantile g-computation (QG-C). BKMR can be used to estimate the exposure-response function, including nonlinear exposure-response curves, linear functions with main effects and their interaction, as well as nonlinear functions incorporating a synergistic interaction between them. The QG-C model considers the nonlinearity and nonadditivity of individual exposures effects and the overall mixture, enabling valid inference on the individual contributions to that metal mixture by calculating the weight of each element in each direction.
In this study, we adopted four novel statistical models, multivariable linear regression, elastic-net regression (ENET), BKMR, and QG-C to evaluate the associations and interactions between individual metals and metal mixtures with blood pressure and to identify important elements that may have the largest contribution to blood pressure alteration in the U.S. general population from the National Health and Nutrition Examination Survey (NHANES) data.

https://doi.org/10.1097/cm9.0000000000002956

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Wang, D., Xia, Z., Wang, L., Yan, J., Yin, H.
Gas Graph Convolutional Transformer for Robust Generalization in Adaptive Gas Mixture Concentration Estimation.
Acs Sensors 2024; Vol. 9 (4) p 1927-1937.

Gas concentration estimation has a tremendous research significance in various fields. However, existing methods for estimating the concentration of mixed gases generally depend on specific data-preprocessing methods and suffer from poor generalizability to diverse types of gases. This paper proposes a graph neural network-based gas graph convolutional transformer model (GGCT)

incorporating the information propagation properties and the physical characteristics of temporal sensor data. GGCT accurately predicts mixed gas concentrations and enhances its generalizability by analyzing the concentration tokens. The experimental results highlight the GGCT's robust performance, achieving exceptional levels of accuracy across most tested gas components, underscoring its strong potential for practical applications in mixed gas analysis.

https://doi.org/10.1021/acssensors.3c02654

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Gerofke, A., Lange, R., Vogel, N., Schmidt, P., Weber, T., David, M.*, et al.*
Phthalates and substitute plasticizers: Main achievements from the European human biomonitoring initiative HBM4EU.
International Journal of Hygiene and Environmental Health 2024; Vol. 259

Phthalates and the substitute plasticizer DINCH belong to the first group of priority substances investigated by the European Human Biomonitoring Initiative (HBM4EU) to answer policy -relevant questions and safeguard an efficient science -to -policy transfer of results. Human internal exposure levels were assessed using two data sets from all European regions and Israel. The first collated existing human biomonitoring (HBM) data (2005 -2019). The second consisted of new data generated in the harmonized "HBM4EU Aligned Studies " (2014 -2021) on children and teenagers for the ten most relevant phthalates and DINCH, accompanied by a quality assurance/ quality control (QA/QC) program for 17 urinary exposure biomarkers. Exposures differed between countries, European regions, age groups and educational levels. Toxicologically derived Human biomonitoring guidance values (HBM-GVs) were exceeded in up to 5% of the participants of the HBM4EU Aligned Studies. A mixture risk assessment (MRA) including five reprotoxic phthalates (DEHP, DnBP, DiBP, BBzP, DiNP) revealed that for about 17% of the children and teenagers, health risks cannot be excluded. Concern about male reproductive health emphasized the need to include other anti -androgenic substances for MRA. Contaminated food and the use of personal care products were identified as relevant exposure determinants paving the way for new regulatory measures. Time trend analyses verified the efficacy of regulations: especially for the highly regulated phthalates exposure dropped significantly, while levels of the substitutes DINCH and DEHTP increased.
The HBM4EU ewaste study, however, suggests that workers involved in e -waste management may be exposed to higher levels of restricted phthalates. Exposure -effect association studies indicated the relevance of a range of endpoints. A set of HBM indicators was derived to facilitate and accelerate science -to -policy transfer. Result indicators allow different groups and regions to be easily compared. Impact indicators allow health risks to be directly interpreted. The presented results enable successful science -to -policy transfer and support timely and targeted policy measures.

https://doi.org/10.1016/j.ijheh.2024.114378

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Dugandzic, R., Konstantelos, N., Yu, Y., Lavigne, E., Srugo, S., Lang, J. J.*, et al.*
Associations between paediatric obesity, chemical mixtures and environmental factors, in a national cross-sectional study of Canadian children.
Pediatric Obesity 14 June 2024.

Background : Whilst single chemical exposures are suspected to be obesogenic, the combined role of chemical mixtures in paediatric obesity is not well understood. Objectives : We aimed to evaluate the potential associations between chemical mixtures and obesity in a population-based sample of Canadian children. Methods : We ascertained biomonitoring and health data for children aged 3-11 from the cross-sectional Canadian Health Measures Survey from 2007 to 2019. Several chemicals of

interest were measured in blood or urine and paediatric obesity was defined based on measured anthropometrics. Using quantile-based G computational analysis, we quantified the effects of three chemical mixtures selected a priori. Models were adjusted for sociodemographic and environmental factors identified through a directed acyclic graph. Results are presented through adjusted relative risks (RR) with 95% confidence intervals (95% CI). Results : We included 9147 children. Of these, 24.1% were overweight or obese. Exposure to the mixture of bisphenol A, acrylamide, glycidamide, metals, parabens and arsenic increased the risk of childhood overweight or obesity by 45% (95% CI 1.09, 1.93), obesity by 109% (95% CI 1.27, 3.42) and central obesity by 82% (95% CI 1.30, 2.56). Conclusions : Our findings support the role of early childhood chemical exposures in paediatric obesity and the potential combined effects of chemicals.

https://doi.org/10.1111/ijpo.13117

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Soleimani, Z., Azimi, P., Haghshenas, R., Farzi, Y., Taherkhani, A., Naddafi, K.*, et al.*
Exposure assessment of metal(loids) in indoor air and biomonitoring in six urban residential areas in Iran.
The Science of the total environment 2024; Vol. 946, p 174169.

Exposure to metal(loid)s can cause adverse health effects. This study evaluated the concentrations of aluminum, arsenic, cadmium, chromium, mercury, nickel, and lead in particulate matter <10mum (PM10) and in the urine of 100 participants from urban residential areas in Iran. A total of 100 residential buildings (one adult from each household) in six cities across Iran were recruited for this study. The levels of metal(loid)s in PM10 and the urine of participants were measured using acid digestion followed by inductively coupled plasma mass spectrometry (ICP-MS). The average (±SE) PM10 concentration in the buildings was 51.7±3.46mug/m3. Aluminum and cadmium had the highest and lowest concentrations among the metal(loid)s, averaging 3.74±1.26mug/m3 and 0.01±0.001mug/m3, respectively. In 85% of the samples, the concentration of metal(loid)s in indoor air exceeded WHO air quality standards. Cadmium and lead had the highest and lowest numbers of indoor air samples exceeding the recommended standards, respectively. A significant correlation was found between the concentration of metal(loid)s in urine samples and indoor PM10 levels, as well as the wealth index of participants. There was also a significant direct relationship between the concentrations of nickel, arsenic, lead, and mercury in urine and the age of participants. Factors such as building location, type of cooling systems, use of printers at home, and natural ventilation influenced the concentration and types of metal(loid)s in the indoor air.

https://doi.org/10.1016/j.scitotenv.2024.174169

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Yang, S. W., Xie, Y., Liu, J.-Z., Zhang, D., Huang, J., Liang, P.
A novel method for quantitative determination of multiple substances using Raman spectroscopy combined with CWT.
Spectrochimica Acta Part a-Molecular and Biomolecular Spectroscopy 5 September 2024; Vol. 317, 124427

The identification of mixed solutions is a challenging and important subject in chemical analysis. In this paper, we propose a novel workflow that enables rapid qualitative and quantitative detection of mixed solutions. We use a methanol -ethanol mixed solution as an example to demonstrate the superiority of this workflow. The workflow includes the following steps: (1) converting Raman spectra into Raman images through CWT; (2) using MobileNetV3 as the backbone network, improved multi -label and multi -channel synchronization enables simultaneous prediction of multiple mixture concentrations; and (3)

using transfer learning and multi -stage training strategies for training to achieve accurate quantitative analysis. We compare six traditional machine learning algorithms and two deep learning models to evaluate the performance of our new method. The experimental results show that our model has achieved good prediction results when predicting the concentration of methanol and ethanol, and the coefficient of determination R 2 is greater than 0.999. At different concentrations, both MAPE and RSD outperform other models, which demonstrates that our workflow has outstanding analytical capabilities. Importantly, we have solved the problem that current quantitative analysis algorithms for Raman spectroscopy are almost unable to accurately predict the concentration of multiple substances simultaneously. In conclusion, it is foreseeable that this non-destructive, automated, and highly accurate workflow can further advance Raman spectroscopy.

https://doi.org/10.1016/j.saa.2024.124427

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Dawson, D. A., Schultz, T. W.
Equations for estimating binary mixture toxicity: 3-methyl-2-butanone with a series of electrophiles.
PLOS ONE 2024; Vol. 19 (7), p e0306382.

Mixture toxicity was determined for 32 binary combinations. One chemical was the non-reactive, non-polar narcotic 3-methyl-2-butanone (always chemical A) and the other was a potentially reactive electrophile (chemical B). Bioluminescence inhibition in Allovibrio fischeri was measured at 15-, 30-, and 45-minutes of exposure for A, B, and the mixture (MX). Concentration-response curves (CRCs) were developed for each chemical and used to develop predicted CRCs for the concentration addition (CA) and independent action (IA) mixture toxicity models. Also, MX CRCs were generated and compared with model predictions using the 45-minute data. Classification of observed mixture toxicity used three specific criteria: 1) predicted IA EC50 vs. CA EC50 values at 45-minutes, 2) consistency of 45-minute MX CRC fit to IA, CA, or otherwise at three effect levels (EC25, EC50 and EC75), and 3) the known/suspected mechanism of toxicity for chemical B. Mixture toxicity was then classified into one of seven groupings. As a result of the predicted IA EC50 being more toxic than the predicted CA EC50, IA represented the greater toxic hazard. For this reason, non-sham MXs having toxicity consistent with CA were classified as being “coincident” with CA rather than mechanistically-consistent with CA. Multiple linear regression analyses were performed to develop equations that can be used to estimate the toxicity of other 3M2B-containing binary mixtures. These equations were developed from the data for both IA and CA, at each exposure duration and effect level. Each equation had a coefficient of determination (r2) above 0.950 and a variance inflation factor <1.2. This approach can potentially reduce the need for mixture testing and is amenable to other model systems and to assays that evaluate toxicity at low effect levels.

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Birolli, W. G., Lanças, F. M., Dos Santos Neto, Á. J., Silveira, H. C. S.
Determination of pesticide residues in urine by chromatography-mass spectrometry: methods and applications.
Frontiers in Public Health 2024; Vol. 12

Pollution has emerged as a significant threat to humanity, necessitating a thorough evaluation of its impacts. As a result, various methods for human biomonitoring have been proposed as vital tools for assessing, managing, and mitigating exposure risks. Among these methods, urine stands out as the most commonly analyzed biological sample and the primary matrix for biomonitoring studies.
Objectives : This review concentrates on exploring the literature concerning residual pesticide

determination in urine, utilizing liquid and gas chromatography coupled with mass spectrometry, and its practical applications.
Method : The examination focused on methods developed since 2010. Additionally, applications reported between 2015 and 2022 were thoroughly reviewed, utilizing Web of Science as a primary resource.
Synthesis : Recent advancements in chromatography-mass spectrometry technology have significantly enhanced the development of multi-residue methods. These determinations are now capable of simultaneously detecting numerous pesticide residues from various chemical and use classes. Furthermore, these methods encompass analytes from a variety of environmental contaminants, offering a comprehensive approach to biomonitoring. These methodologies have been employed across diverse perspectives, including toxicological studies, assessing pesticide exposure in the general population, occupational exposure among farmers, pest control workers, horticulturists, and florists, as well as investigating consequences during pregnancy and childhood, neurodevelopmental impacts, and reproductive disorders. Future directions : Such strategies were essential in examining the health risks associated with exposure to complex mixtures, including pesticides and other relevant compounds, thereby painting a broader and more accurate picture of human exposure. Moreover, the implementation of integrated strategies, involving international research initiatives and biomonitoring programs, is crucial to optimize resource utilization, enhancing efficiency in health risk assessment.

https://doi.org/10.3389/fpubh.2024.1336014

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Feng, Z., Chen, Y. A., Guo, Y., Lyu, J.
Deciphering the environmental chemical basis of muscle quality decline by interpretable machine learning models.
The American Journal of Clinical Nutrition 2024; Vol., p

Background Sarcopenia is known as a decline in skeletal muscle quality and function that is associated with age. Sarcopenia is linked to diverse health problems, including endocrine-related diseases. Environmental chemicals (ECs), a broad class of chemicals released from industry, may influence muscle quality decline. Objective In our work, we aim to simultaneously elucidate the associations between muscle quality decline and diverse EC exposures based on the data from the 2011–2012 and 2013–2014 survey cycles in the National Health and Nutrition Examination Survey (NHANES) project using machine learning models. Methods Six machine learning models were trained based on the EC and non-EC exposures from NHANES to distinguish low from normal muscle quality index status. Different machine learning metrics were evaluated for these models. The SHAP (SHapley Additive exPlanations) approach was used to provide explainability for machine learning models.
Results Random Forest (RF) performed best on the independent testing dataset. Based on the testing dataset, ECs can independently predict the binary muscle quality status with good performance by RF (Area Under the Receiver Operating Characteristic Curve (AUROC) = 0.793, Area Under the Precision-Recall Curve (AUPRC) = 0.808). The SHAP ranked the importance of ECs for the RF model. As a result, several metals and chemicals in urine, including 3-phenoxybenzoic acid and cobalt, were more associated with the muscle quality decline.
Conclusions Altogether, our analyses suggest that ECs can independently predict muscle quality decline with a good performance by RF, and the SHAP-identified ECs can be closely related to muscle quality decline and sarcopenia. Our analyses may provide valuable insights into environmental chemicals that may be the important basis of sarcopenia and endocrine-related diseases in U.S. populations.

https://doi.org/https://doi.org/10.1016/j.ajcnut.2024.05.022

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Guimbaud, J.-B., Siskos, A. P., Sakhi, A. K., Heude, B., Sabido, E., Borras, E.*, et al.*
Machine learning-based health environmental-clinical risk scores in European children.
Communications Medicine 2024; Vol. 4 (1)

Background Early life environmental stressors play an important role in the development of multiple chronic disorders. Previous studies that used environmental risk scores (ERS) to assess the cumulative impact of environmental exposures on health are limited by the diversity of exposures included, especially for early life determinants. We used machine learning methods to build early life exposome risk scores for three health outcomes using environmental, molecular, and clinical data.
Methods In this study, we analyzed data from 1622 mother-child pairs from the HELIX European birth cohorts, using over 300 environmental, 100 child peripheral, and 18 mother-child clinical markers to compute environmental-clinical risk scores (ECRS) for child behavioral difficulties, metabolic syndrome, and lung function. ECRS were computed using LASSO, Random Forest and XGBoost. XGBoost ECRS were selected to extract local feature contributions using Shapley values and derive feature importance and interactions.
Results ECRS captured 13%, 50% and 4% of the variance in mental, cardiometabolic, and respiratory health, respectively. We observed no significant differences in predictive performances between the above-mentioned methods. The most important predictive features were maternal stress, noise, and lifestyle exposures for mental health; proteome (mainly IL1B) and metabolome features for cardiometabolic health; child BMI and urine metabolites for respiratory health.
Conclusions Besides their usefulness for epidemiological research, our risk scores show great potential to capture holistic individual level non-hereditary risk associations that can inform practitioners about actionable factors of high-risk children. As in the post-genetic era personalized prevention medicine will focus more and more on modifiable factors, we believe that such integrative approaches will be instrumental in shaping future healthcare paradigms. Growing up in different environments can greatly affect children's health later in life. This research looked at how living in cities, being exposed to chemicals, and other experiences before birth and during childhood, work together to influence children's mental, cardiovascular and respiratory health. We used advanced computer programs to help us understand these effects and estimate health risk scores. These scores are simple numerical measures that help us quantify the likelihood of children developing health issues based on their environmental exposures. Using those scores, the study identified key factors impacting children's health, in particular psycho-social, perceived environmental and prenatal pollutant exposures for mental health. It also revealed complex patterns and interactions between environmental factors. The results highlighted the potential of such risk scores to support the identification of actionable factors in high-risk children, informing tailored prevention measures in healthcare. Guimbaud et al. use machine learning in a dataset of 1600 European mother-child pairs to link early-life environmental exposures with children's health. Through the computation of environmental-clinical risk scores, they unveil complex interactions and nonlinear patterns among these factors, underscoring their intricate role in children's health.

https://doi.org/10.1038/s43856-024-00513-y

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Hu, C.-W., Chang, Y.-J., Chang, W.-H., Cooke, M. S., Chen, Y.-R., Chao, M.-R.
A Novel Adductomics Workflow Incorporating FeatureHunter Software: Rapid Detection of Nucleic Acid Modifications for Studying the Exposome.
Environmental science & technology 2024; Vol. 58 (1), p 75-89.

Exposure to the physicochemical agents that interact with nucleic acids (NA) may lead to modification of DNA and RNA (i.e., NA modifications), which have been associated with various diseases, including cancer. The emerging field of NA adductomics aims to identify both known and unknown NA

modifications, some of which may also be associated with proteins. One of the main challenges for adductomics is the processing of massive and complex data generated by high-resolution tandem mass spectrometry (HR-MS/MS). To address this, we have developed a software called "FeatureHunter", which provides the automated extraction, annotation, and classification of different types of key NA modifications based on the MS and MS/MS spectra acquired by HR-MS/MS, using a user-defined feature list. The capability and effectiveness of FeatureHunter was demonstrated by analyzing various NA modifications induced by formaldehyde or chlorambucil in mixtures of calf thymus DNA, yeast RNA and proteins, and by analyzing the NA modifications present in the pooled urines of smokers and nonsmokers. The incorporation of FeatureHunter into the NA adductomics workflow offers a powerful tool for the identification and classification of various types of NA modifications induced by reactive chemicals in complex biological samples, providing a valuable resource for studying the exposome.

https://doi.org/10.1021/acs.est.3c04674

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Co-expositions aux métaux lourds (et effets sur la santé)

Yang, X., Li, L., Nie, L.
Associations between co-exposure to heavy metals and vertebral compression fracture, as well as femoral neck bone mineral density: A cross-sectional study from NHANES data.
Plos One 2024; Vol. 19 (5)

Objective Accumulating evidence showed that exposure to heavy metals was harmful to human health. Little is known regarding the mixing effects of multiple metal exposures on vertebral compression fracture (VCF) and femoral neck bone mineral density (BMD). This study aimed to explore the individual and joint effects of four heavy metals [manganese (Mn), lead (Pb), cadmium (Cd) and mercury (Hg)] on VCF risk and femoral neck BMD.
Methods This cross-sectional study included 1,007 eligible individuals with vertebral fractures from National Health and Nutrition Examination Survey 2013-2014. The outcome was the risk of VCF and femoral neck BMD. Weighted multivariate logistic regression was used to explore the individual effect of four heavy metals on the VCF risk, separately. Weighted multivariate linear regression was used to explore the individual effect of four heavy metals on the femoral neck BMD, separately. Adopted bayesian kernel machine regression (BKMR) model and quantile-based g computation (qgcomp) to examine the joint effects of four heavy metals on the VCF risk and femoral neck BMD.
Results Among the population, 57 individuals developed VCF. After adjusting covariates, we found no statistical differences regarding the individual effects of four heavy metals on the risk of VCF. BKMR model and qgcomp indicated that there were no statistical differences regarding the joint effects between four heavy metals on the VCF risk. In addition, we found that Cd was associated with femoral neck BMD, and an increase in the mixture of heavy metal exposures was associated with a decreased risk of femoral neck BMD. Conclusion No significant correlation was observed between co-exposure to Mn, Pb, Cd and Hg and VCF risk. But co-exposure to Mn, Pb, Cd and Hg may be associated with femoral neck BMD.

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Ngwa, H. A., Bargues-Carot, A., Jin, H., Anantharam, V., Kanthasamy, A., Kanthasamy, A. G.
Manganese and Vanadium Co-Exposure Induces Severe Neurotoxicity in the Olfactory System: Relevance to Metal-Induced Parkinsonism.
International Journal of Molecular Sciences 2024; Vol. 25 (10)

Chronic environmental exposure to toxic heavy metals, which often occurs as a mixture through occupational and industrial sources, has been implicated in various neurological disorders, including Parkinsonism. Vanadium pentoxide (V2O5) typically presents along with manganese (Mn), especially in welding rods and high-capacity batteries, including electric vehicle batteries; however, the neurotoxic effects of vanadium (V) and Mn co-exposure are largely unknown. In this study, we investigated the neurotoxic impact of MnCl2, V2O5, and MnCl2-V2O5 co-exposure in an animal model. C57BL/6 mice were intranasally administered either de-ionized water (vehicle), MnCl2 (252 mu g) alone, V2O5 (182 mu g) alone, or a mixture of MnCl2 (252 mu g) and V2O5 (182 mu g) three times a week for up to one month. Following exposure, we performed behavioral, neurochemical, and histological studies. Our results revealed dramatic decreases in olfactory bulb (OB) weight and levels of tyrosine hydroxylase, dopamine, and 3,4-dihydroxyphenylacetic acid in the treatment groups compared to the control group, with the Mn/V co-treatment group producing the most significant changes. Interestingly, increased levels of alpha-synuclein expression were observed in the substantia nigra (SN) of treated animals. Additionally, treatment groups exhibited locomotor deficits and olfactory dysfunction, with the co-treatment group producing the most severe deficits. The treatment groups exhibited increased levels of the oxidative stress marker 4-hydroxynonenal in the striatum and SN, as well as the upregulation of the pro-apoptotic protein PKC delta and accumulation of glomerular astroglia in the OB. The co-exposure of animals to Mn/V resulted in higher levels of these metals compared to other treatment groups. Taken together, our results suggest that co-exposure to Mn/V can adversely affect the olfactory and nigral systems. These results highlight the possible role of environmental metal mixtures in the etiology of Parkinsonism.

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Iskandar, I. Y. K., Gawkrodger, D. J., Byrne, L., Gittins, M., Carder, M., Fishwick, D., Van Tongeren, M.
Trends in work-related respiratory diseases attributed to nickel, chromium and cobalt in the UK: descriptive findings from The Health and Occupation Research (THOR) network 1996-2019.
Occupational and Environmental Medicine 2024; Vol. 81 (4), p 220-224.

Background Occupational exposure to metals can be associated with respiratory diseases which can adversely affect the individual's health, finances and employment. Despite this, little is known about the incidence of these respiratory conditions over prolonged periods of time. Aims : This study aimed to investigate the trends in the incidence of work-related respiratory diseases attributed to nickel, chromium and cobalt in the UK.
Methods : Cases of occupational respiratory diseases caused by nickel, chromium or cobalt reported to Surveillance of Work-related and Occupational Respiratory Disease (SWORD), the UK-based surveillance scheme between 1996 and 2019 (inclusive), were extracted and grouped into six 4-year time periods. Cases were characterised by causative metal exposure, occupational and industrial sector. Incidence rates diseases (adjusted for physician participation and response rate) were calculated using ONS employment data.
Results : Of cases reported to SWORD during the study period, 1% (173 actual cases) of respiratory problems were attributed to nickel, chromium or cobalt. Diagnoses of asthma compromised the largest proportion of diagnoses (74.4%), followed by lung cancer (8.9%) and pneumoconiosis (6.7%). Cases had a mean age of 47 years (SD 13); 93% were men. The annual incidence fell from 1.6 per million employed in the first 4-year period, to 0.2 in the most recent period.
Conclusions Over 24 years, a decline in the incidence of metal-related occupational respiratory

diseases was observed in the UK. This could be attributed to improvements in working conditions which resulted in reduced metal exposure but could also be due to closure of industries that might have generated case returns.

https://doi.org/10.1136/oemed-2023-109066

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Shi, X., Wang, X., Zhang, J., Dang, Y., Ouyang, C., Pan, J.*, et al.*
Associations of mixed metal exposure with chronic kidney disease from NHANES 2011-2018.
Scientific reports 2024; Vol. 14 (1), p 13062-13062.

Metals have been proved to be one of risk factors for chronic kidney disease (CKD) and diabetes, but the effect of mixed metal co-exposure and potential interaction between metals are still unclear. We assessed the urine and whole blood levels of cadmium (Cd), manganese (Mn), lead (Pb), mercury (Hg), and renal function in 3080 adults from National Health and Nutrition Survey (NHANES) (2011-2018) to explore the effect of mixed metal exposure on CKD especially in people with type 2 diabetes mellitus (T2DM). Weighted quantile sum regression model and Bayesian Kernel Machine Regression model were used to evaluate the overall exposure impact of metal mixture and potential interaction between metals.
The results showed that the exposure to mixed metals was significantly associated with an increased risk of CKD in blood glucose stratification, with the risk of CKD being 1.58 (1.26,1.99) times in urine and 1.67 (1.19,2.34) times in whole blood higher in individuals exposed to high concentrations of the metal mixture compared to those exposed to low concentrations. The effect of urine metal mixture was elevated magnitude in stratified analysis. There were interactions between urine Pb and Cd, Pb and Mn, Pb and Hg, Cd and Mn, Cd and Hg, and blood Pb and Hg, Mn and Cd, Mn and Pb, Mn and Hg on the risk of CKD in patients with T2DM and no significant interaction between metals was observed in non-diabetics.
In summary, mixed metal exposure increased the risk of CKD in patients with T2DM, and there were complex interactions between metals. More in-depth studies are needed to explore the mechanism and demonstrate the causal relationship.

https://doi.org/10.1038/s41598-024-63858-3

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Liu, Y., Jin, Z., Fu, S.
Threshold and combined effects of heavy metals on the risk of phenotypic age acceleration among U.S. adults.
Biometals 2024.

Accumulation of heavy metals in the body has been shown to affect the phenotypic age (PhenoAge). However, the combined and threshold effects of blood heavy metals on the risk of PhenoAge acceleration (PhenoAgeAccel) are not well understood. A cross-sectional study was conducted using blood heavy metal data (N = 7763, age ≥18 years) from the 2015-2018 National Health and Nutrition Examination Survey. PhenoAgeAccel was calculated from actual age and nine biomarkers. Multiple regression equations were used to describe the relationship between heavy metals and PhenoAgeAccel. Least Absolute Shrinkage and Selection Operator (LASSO) regression modeling was used to explore the relationship between the combined effects of heavy metals and PhenoAgeAccel. Threshold effect and multiple regression analyses were performed to explore the linear and nonlinear relationships between heavy metals and PhenoAgeAccel. Threshold effect analysis showed that blood mercury (Hg) concentration was linearly associated with PhenoAgeAccel. In contrast, lead (Pb), cadmium (Cd), manganese (Mn), and combined exposure were nonlinearly associated with

PhenoAgeAccel. In addition, the combination of Pb, Cd, Hg, and Mn significantly affected PhenoAgeAccel. The risk of PhenoAgeAccel was increased by 207% (P < 0.0001). Meanwhile, a threshold relationship was found between blood Pb, Cd, Mn, and the occurrence of PhenoAgeAccel. Overall, our results indicate that combined exposure to heavy metals may increase the risk of PhenoAgeAccel. This study underscores the need to reduce heavy metal pollution in the environment and provides a reference threshold for future studies.

https://doi.org/10.1007/s10534-024-00609-x

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Dos Reis, L. L., De Abreu, C. B., Gebara, R. C., Rocha, G. S., Longo, E., Mansano, A. D. S., Melao, M. D. G. G.
Effects of Cadmium and Nickel Mixtures on Multiple Endpoints of the Microalga *Raphidocelis subcapitata*.
Environmental Toxicology and Chemistry 2024 :1-15. (c) 2024 SETAC

It is crucial to investigate the effects of mixtures of contaminants on aquatic organisms, because they reflect what occurs in the environment. Cadmium (Cd) and nickel (Ni) are metals that co-occur in aquatic ecosystems, and information is scarce on their joint toxicity to Chlorophyceae using multiple endpoints. We evaluated the effects of isolated and combined Cd and Ni metals on multiple endpoints of the chlorophycean Raphidocelis subcapitata. The results showed that Cd inhibited cell density, increased reactive oxygen species (ROS) production (up to 308% at 0.075 mg L-1 of Cd), chlorophyll a (Chl a) fluorescence (0.050-0.100 mg L-1 of Cd), cell size (0.025-0.100 mg L-1 of Cd), and cell complexity in all concentrations evaluated. Nickel exposure decreased ROS production by up to 25% at 0.25 mg L-1 of Ni and Chl a fluorescence in all concentrations assessed. Cell density and oxygen-evolving complex (initial fluorescence/variable fluorescence [F-0/F-v]) were only affected at 0.5 mg L-1 of Ni. In terms of algal growth, mixture toxicity showed antagonism at low doses and synergism at high doses, with a dose level change greater than the median inhibitory concentration. The independent action model and dose-level-dependent deviation best fit our data. Cadmium and Ni mixtures resulted in a significant increase in cell size and cell complexity, as well as changes in ROS production and Chl a fluorescence, and they did not affect the photosynthetic parameters.

https://doi.org/10.1002/etc.5927

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Tang, C., Wang, Y., Hong, H.
Unraveling the link between heavy metals, perfluoroalkyl substances and depression: Insights from epidemiological and bioinformatics strategies.
Ecotoxicology and Environmental Safety 2024; Vol. 279, 1 July 2024, 116482

Heavy metals and per- and polyfluoroalkyl substances (PFASs) have become particularly important when studying the development of depression, a common illness that severely restricts psychosocial functioning and diminishes quality of life. Therefore, the potential joint effects of heavy metal and PFAS exposure on depression, as well as the underlying mechanisms involved, were investigated by using integrated epidemiological and bioinformatic approaches in the present study. A thorough analysis of 7301 samples from the National Health and Nutrition Examination Survey (NHANES) cycles that occurred between 2005 and 2018 was performed. Single-exposure studies have shown that cadmium exposure is positively associated with depression, whereas perfluorooctanesulfonic acid (PFOS) exposure and perfluorodecanoic acid (PFDE) exposure are negatively associated with depression. Furthermore, the Bayesian kernel machine regression (BKMR) and quantile gcomputation

(QGcomp) models were employed to investigate the collective impact of exposure to mixed metals on depression. Cadmium emerged as the principal contributor to depression. Moreover, the addition of PFAS to the metal mixture had an antagonistic effect on depression, with PFOS having the most prominent influence. Analysis of the effects of co-exposure to cadmium and PFOS confirmed the presence of an antagonistic effect. The inflection points of cadmium and PFOS were determined to be -1.11 and 2.27, respectively. Additionally, exposure to cadmium and PFOS had the opposite effects on two crucial pathways, namely, the rap1 and calcium signaling pathways, which involve core genes related to depression such as ADORA2A, FGF2, and FGFR1. These findings have significant implications for future studies and provide new strategies for exploring the mechanisms underlying co-exposure effects.

https://doi.org/10.1016/j.ecoenv.2024.116482

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Lin, J. J. Y., Kuiper, J. R., Dickerson, A. S., Buckley, J. P., Volk, H. E., Rohlman, D. S.*, et al.*
Associations of a toenail metal mixture with attention and memory in the Gulf long-term follow-up (GuLF) study.
Science of the Total Environment 20 July 2024; Vol. 935, 173387

Background: Research on metal-associated neurodegeneration has largely focused on single metals. Since metal exposures typically co-occur as combinations of both toxic and essential elements, a mixtures framework is important for identifying risk and protective factors. This study examined associations between toenail levels of an eight-metal mixture and attention and memory in men living in US Gulf states.
Methods: We measured toenail concentrations of toxic (arsenic, chromium, lead, and mercury) and essential (copper, manganese, selenium, and zinc) metals in 413 non-smoking men (23-69 years, 46 % Black) from the Gulf Long-Term Follow-Up (GuLF) Study. Sustained attention and working memory were assessed at the time of toenail sample collection using the continuous performance test (CPT) and digit span test (DST), respectively. Associations between toenail metal concentrations and performance on neurobehavioral tests were characterized using co -pollutant adjusted general linear models and Bayesian Kernel Machine Regression.
Results: Adjusting for other metals, one interquartile range (IQR) increase in toenail chromium was associated with a 0.19 (95 % CI: -0.31, -0.07) point reduction in CPT D Prime score (poorer ability to discriminate test signals from noise). One IQR increase in toenail manganese was associated with a 0.20 (95 % CI, -0.41, 0.01) point reduction on the DST Reverse Count (fewer numbers recalled). Attention deficits were greater among Black participants compared to White participants for the same increase in toenail chromium concentrations. No ev- idence of synergistic interaction between metals or adverse effect of the overall metal mixture was observed for either outcome.
Conclusions: Our findings support existing studies of manganese -related memory deficits and are some of the first to show chromium related attention deficits in adults. Longitudinal study of cognitive decline is needed to verify chromium findings. Research into social and chemical co -exposures is also needed to explain racial differences in metal -associated neurobehavioral deficits observed in this study.

https://doi.org/10.1016/j.scitotenv.2024.173387

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Herruzo-Ruiz, A. M., Trombini, C., Moreno-Garrido, I., Blasco, J., Alhama, J., Michan, C.
Ions and nanoparticles of Ag and/or Cd metals in a model aquatic microcosm: Effects on the abundance, diversity and functionality of the sediment bacteriome.
Marine Pollution Bulletin July 2024; Vol. 204, 116525

Metals can be adsorbed on particulate matter, settle in sediments and cause alterations in aquatic environments. This study assesses the effect of Ag and/or Cd, both in ionic and nanoparticle (NP) forms, on the microbiome of sediments. For that purpose, aquatic controlled -microcosm experiments were exposed to an environmentally relevant and at tenfold higher doses of each form of the metals. Changes in the bacteriome were inferred by 16S rDNA sequencing. Ionic Ag caused a significant decrease of several bacterial families, whereas the effect was opposite when mixed with Cd, e.g., Desulfuromonadaceae family; in both cases, the bacteriome functionalities were greatly affected, particularly the nitrogen and sulfur metabolism. Compared to ionic forms, metallic NPs produced hardly any change in the abundance of microbial families, although the alpha-biodiversity of the bacteriome was reduced, and the functionality altered, when exposed to the NPs<acute accent>mixture. Our goal is to understand how metals, in different forms and combinations, released into the environment may endanger the health of aquatic ecosystems. This work may help to understand how aquatic metal pollution alters the structure and functionality of the microbiome and biogeochemical cycles, and how these changes can be addressed.

https://doi.org/10.1016/j.marpolbul.2024.116525

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Fu, M., Zhu, Z., Xiang, Y., Yang, Q., Yuan, Q., Li, X., Yu, G.
Associations of Blood and Urinary Heavy Metals with Stress Urinary Incontinence Risk Among Adults in NHANES, 2003-2018.
Biological Trace Element Research 2024

People come into contact with heavy metals in various ways in their daily lives. Accumulating evidence shows that toxic metal exposure is hazardous to human health. However, limited information is available regarding the impact of metal mixtures on stress urinary incontinence (SUI). Therefore, we used data from 10,622 adults from the 2003-2018 National Health and Nutrition Examination Survey (NHANES) to investigate the independent and comprehensive association between heavy metal co-exposure and SUI. Among them, 2455 (23.1%) had been diagnosed with SUI, while the rest had no SUI. We evaluated the independent and combined associations of 3 blood metals and 10 urinary metals with SUI risk, along with subgroup analyses according to age and gender. In the single-exposure model, blood cadmium (Cd), lead (Pb), mercury (Hg), urinary Cd, Pb, and cesium (Cs) were found to be positively connected with SUI risk. Moreover, weighted quantile sum (WQS) regression, quantile-based g-computation (qgcomp), and Bayesian kernel machine regression (BKMR) consistently demonstrated blood and urinary metal-mixed exposure were positively associated with the risk of SUI, and emphasized that blood Pb and Cd and urinary Cd and Cs were the main positive drivers, respectively. This association was more pronounced in the young and middle-aged group (20-59 years old) and the female group. Nevertheless, further research is necessary to validate these significant findings.

https://doi.org/10.1007/s12011-024-04264-8

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Wu, T., Luo, C., Li, T., Zhang, C., Chen, H.-X., Mao, Y.-T.*, et al.*
Effects of exposure to multiple metallic elements in the first trimester of pregnancy on the risk of preterm birth.
Maternal & Child Nutrition Vol. n/a (n/a) p e13682.

Abstract Exposure to certain heavy metals has been demonstrated to be associated with a higher risk of preterm birth (PTB). However, studies focused on the effects of other metal mixtures were limited. A nested case–control study enrolling 94 PTB cases and 282 controls was conducted. Metallic elements were detected in maternal plasma collected in the first trimester using inductively coupled plasma–mass spectrometry. The effect of maternal exposure on the risk of PTB was investigated using logistic regression, least absolute shrinkage and selection operator, restricted cubic spline (RCS), quantile g computation (QGC) and Bayesian kernel machine regression (BKMR). Vanadium (V) and arsenic (As) were positively associated with PTB risk in the logistic model, and V remains positively associated in the multi-exposure logistic model. QGC analysis determined V (69.42%) and nickel (Ni) (70.30%) as the maximum positive and negative contributors to the PTB risk, respectively. BKMR models further demonstrated a positive relationship between the exposure levels of the mixtures and PTB risk, and V was identified as the most important independent variable among the elements. RCS analysis showed an inverted U-shape effect of V and gestational age, and plasma V more than 2.18 μg/L was considered a risk factor for shortened gestation length. Exposure to metallic elements mixtures consisting of V, As, cobalt, Ni, chromium and manganese in the first trimester was associated with an increased risk of PTB, and V was considered the most important factor in the mixtures in promoting the incidence of PTB.

https://doi.org/https://doi.org/10.1111/mcn.13682

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Kabir, E., Shila, T. T., Islam, J., Beauty, S. A., Islam, F., Hossain, S.*, et al.*
Concomitant Exposure to Lower Doses of Arsenic, Lead, and Manganese Induces Greater Synergistic Neurotoxicity Than Individual Metals in Mice.
Biological Trace Element Research 2024;

People in Bangladesh are often exposed to low to high levels of multiple metals due to contaminated groundwater with various heavy metals such as arsenic (As), lead (Pb), and manganese (Mn). However, the effects of concomitant exposure of these three metals on neurobehavioral changes are yet to be studied. Therefore, this study was intended to assess the neurotoxic effect of As, Pb, and Mn in a mouse model. Elevated plus maze (EPM) and Morris water maze (MWM) tests were conducted to evaluate anxiety, learning, and spatial memory impairment, respectively. The mice exposed to a combination of metals spent least time exploring the open arms and had longer latencies to find the hidden platform than the control and individual metal exposure groups in EPM and MWM tests. Moreover, concomitant multi-metal exposure remarkably decreased the activities of cholinergic and antioxidant enzymes, brain-derived neurotropic factor (BDNF), and nuclear factor erythroid 2–related factor 2 (Nrf2) levels and significantly increased interleukin-6 (IL-6) level in the brain tissue compared to the control and individual metal-exposed mice. Among the mice treated with a single metal, the As-treated mice showed the highest toxic effects than Pb- or Mn-treated mice. Taken together, the present study demonstrated that exposure to a mixture of As, Pb, and Mn, even at lower doses than individual metals, significantly augmented anxiety-like behavior and impaired learning and spatial memory compared to exposure to individual metals, which was associated with the changes of BDNF, Nrf2, IL-6 levels, and related enzyme activities in the brain.

https://doi.org/10.1007/s12011-024-04260-y

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Li, H., Cheng, B.-J., Yang, P.-Y., Wang, C., Meng, K., Li, T.-L.*, et al.*
Associations of Urinary Heavy Metal Mixtures with High Remnant Cholesterol among US Adults: Evidence from the National Health and Nutrition Examination Survey (1998–2018).
Toxics 2024; Vol. 12 (6), p 430.

The main objective of our study is to explore the associations between combined exposure to urinary heavy metals and high remnant cholesterol (HRC), a known cardiovascular risk factor. Utilizing data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018, we conducted a cross-sectional analysis of 5690 participants, assessing urinary concentrations of ten heavy metals. Ten heavy metals in urine were measured by inductively coupled plasma mass spectrometry (ICP-MS). Fasting residual cholesterol ≥0.8 mmol/L was defined as HRC (using blood samples). Statistical analyses included weighted multivariable logistic regression, weighted quantile sum (WQS) regression, quantile g-computation (qgcomp), and Bayesian kernel machine regression (BKMR) to evaluate the associations of heavy metal exposure with HRC. Stratified analyses based on individual characteristics were also conducted. Multivariable logistic regression found that the four metals (OR Q4 vs. Q1: 1.33, 95% CI: 1.01–1.75 for barium (Ba); OR Q4 vs. Q1: 1.50, 95% CI: 1.16–1.94 for cadmium (Cd); OR Q4 vs. Q1: 1.52, 95% CI: 1.15–2.01 for mercury (Hg); OR Q4 vs. Q1: 1.35, 95% CI: 1.06–1.73 for lead (Pb)) were positively correlated with the elevated risk of HRC after adjusting for covariates. In addition, all three mixed models, including WQS (OR: 1.25; 95% CI: 1.07–1.46), qgcomp (OR: 1.17; 95% CI: 1.03–1.34), and BKMR, consistently showed a significant positive correlation between co-exposure to heavy metal mixtures and HRC, with Ba and Cd being the main contributors within the mixture. These associations were more pronounced in younger adults (20 to 59 years), males, and those with a higher body mass index status (≥25 kg/m2). Our findings reveal a significant relationship between exposure to the mixture of heavy metals and HRC among US adults, with Ba and Cd being the major contributors to the mixture's overall effect. Public health efforts aimed at reducing heavy metal exposure can help prevent HRC and, in turn, cardiovascular disease.

https://www.mdpi.com/2305-6304/12/6/430

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Pálešová, N., Řiháčková, K., Kuta, J., Pindur, A., Šebejová, L., Čupr, P.
Internal Flames: Metal(loid) Exposure Linked to Alteration of the Lipid Profile in Czech Male Firefighters (CELSPAC-FIREexpo Study).
Environmental Science & Technology Letters 2024.

Increased wildfire activity increases the demands on fire rescue services and firefighters' contact with harmful chemicals. This study aimed to determine firefighters' exposure to toxic metal(loid)s and its association with the lipid profile. CELSPAC-FIREexpo study participants (including 110 firefighters) provided urine and blood samples to quantify urinary levels of metal(loid)s (arsenic, cadmium (Cd), mercury, and lead (Pb)), and serum lipid biomarkers (cholesterol (CHOL), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglycerides (TG)). The associations were investigated by using multiple linear regression and Bayesian weighted quantile sum (BWQS) regression. Higher levels of Pb were observed in firefighters. Pb was positively associated with CHOL and TG. Cd was negatively associated with HDL. In the BWQS model, the mixture of metal(loid)s was associated positively with CHOL (β = 14.75, 95% CrI = 2.45–29.08), LDL (β = 15.14, 95% CrI = 3.39–29.35), and TG (β = 14.79, 95% CrI = 0.73–30.42), while negatively with HDL (β = −14.96, 95% CrI = −25.78 to −1.8). Pb emerged as a key component in a metal(loid) mixture. The results suggest that higher exposure to lead and the mixture of metal(loid)s is associated with the alteration of the lipid profile, which can result in an unfavorable cardiometabolic profile, especially in occupationally exposed firefighters.

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Qiu, Y., Liu, Y., Gan, M., Wang, W., Jiang, T., Jiang, Y.*, et al.*
Association of prenatal multiple metal exposures with child neurodevelopment at 3 years of age: A prospective birth cohort study.
Science of The Total Environment 10 September 2024, Vol. 942 ; 173812.

Prenatal exposures to toxic metals and trace elements have been linked to childhood neurodevelopment. However, existing evidence remains inconclusive, and further research is needed to investigate the mixture effects of multiple metal exposures on childhood neurodevelopment. We aimed to examine the associations between prenatal exposure to specific metals and metal mixtures and neurodevelopment in children. In this prospective cohort study, we used the multivariable linear regressions and the robust modified Poisson regressions to explore the associations of prenatal exposure to 25 specific metals with neurodevelopment among children at 3 years of age in 854 mother-child pairs from the Jiangsu Birth Cohort (JBC) Study. The Bayesian kernel machine regression (BKMR) was employed to assess the joint effects of multiple metals on neurodevelopment. Prenatal manganese (Mn) exposure was negatively associated with the risk of non-optimal cognition development of children, while vanadium (V), copper (Cu), zinc (Zn), antimony (Sb), cerium (Ce) and uranium (U) exposures were positively associated with the risk of non-optimal gross motor development. BKMR identified an interaction effect between Sb and Ce on non-optimal gross motor development. Additionally, an element risk score (ERS), representing the mixture effect of multiple metal exposures including V, Cu, Zn, Sb, Ce and U was constructed based on weights from a Poisson regression model. Children with ERS in the highest tertile had higher probability of non-optimal gross motor development (RR = 2.37, 95 % CI: 1.15, 4.86) versus those at the lowest tertile. Notably, Sb [conditional-posterior inclusion probabilities (cPIP) = 0.511] and U (cPIP = 0.386) mainly contributed to the increased risk of non-optimal gross motor development. The findings highlight the importance of paying attention to the joint effects of multiple metals on children's neurodevelopment. The ERS score may serve as an indicator of comprehensive metal exposure risk for children's neurodevelopment.

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Métabolites, biomarqueurs et multi-expositions chimiques

Yang, R., Sun, F., Pan, X.-F., Su, Y., Wu, P., Yuan, J.*, et al.*
Metal exposure and blood lipid biomarkers in early pregnancy: A cross-sectional study.
Environmental Pollution 2024; Vol. 355, p 124238.

Recognizing the risk factors for dyslipidemia during pregnancy is crucial for safeguarding the health of both the mothers and the offspring. Growing evidence emerged and suggested links between environmental factors, including metals, and alteration in lipid levels or dyslipidemia in general populations. However, knowledge of the associations during pregnancy remains extremely lacking. Herein, we aimed to explore whether elevated metal exposure constitutes a risk factor for dyslipidemia in pregnant women. Based on the Tongji-Shuangliu Birth Cohort (TSBC), a total of 663 pregnant women were recruited and their urinary levels of 17 metals and blood lipid biomarkers in early pregnancy were measured, namely triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). The multivariable linear regression models revealed

that exposure to selected metals during early pregnancy was significantly associated with some important biomarkers. In particular, after natural log-transformed for the levels of lipid biomarkers and metals, copper (Cu) exposure was positively associated with HDL-C (β = 0.024, 95% CI: 0.001, 0.046), while zinc (Zn) was associated with TG (β = 0.062, 95% CI: 0.013, 0.110) and selenium with TC (β = 0.028, 95% CI: 0.004, 0.054). Exposure to rubidium (Rb) was positively associated with multiple lipid biomarkers, including HDL-C (β = 0.020, 95% CI: 0.002, 0.037) and LDL-C (β = 0.022, 95% CI: 0.001, 0.042). Mixture exposure analysis further identified significant associations between Cu and HDL-C, Zn and TG, Rb and HDL-C, when multiple metal exposures were considered in the Bayesian kernel machine regression model simultaneously. Our findings showed that exposure to several metals during early pregnancy was associated with an increased prevalence of blood lipid abnormalities in pregnant women. These findings underscore the potential impact of metal combinations on lipid metabolism and increase our understanding of the risk factors associated with abnormal lipid metabolism during pregnancy.

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Wu, Y., Qi, M., Yu, H., Li, G., An, T.
Assessment of internal exposure risk from metals pollution of occupational and non-occupational populations around a non-ferrous metal smelting plant.
Journal of Environmental Sciences 2025; Vol. 147, p 62-73.

Non-ferrous metal smelting poses significant risks to public health. Specifically, the copper smelting process releases arsenic, a semi -volatile metalloid, which poses an emerging exposure risk to both workers and nearby residents. To comprehensively understand the internal exposure risks of metal(loid)s from copper smelting, we explored eighteen metal(loid)s and arsenic metabolites in the urine of both occupational and non -occupational populations using inductively coupled plasma mass spectrometry with high-performance liquid chromatography and compared their health risks. Results showed that zinc and copper (485.38 and 14.00 mu g/L), and arsenic, lead, cadmium, vanadium, tin and antimony (46.80, 6.82, 2.17, 0.40, 0.44 and 0.23 mu g/L, respectively) in workers (n = 179) were significantly higher compared to controls (n = 168), while Zinc, tin and antimony (412.10, 0.51 and 0.15 mu g/L, respectively) of residents were significantly higher than controls. Additionally, workers had a higher monomethyl arsenic percentage (MMA%), showing lower arsenic methylation capacity. Source appointment analysis identified arsenic, lead, cadmium, antimony, tin and thallium as co -exposure metal(loid)s from copper smelting, positively relating to the age of workers. The hazard index (HI) of workers exceeded 1.0, while residents and control were approximately at 1.0. Besides, all three populations had accumulated cancer risks exceeding 1.0 x 10-4, and arsenite (AsIII) was the main contributor to the variation of workers and residents. Furthermore, residents living closer to the smelting plant had higher health risks. This study reveals arsenic exposure metabolites and multiple metals as emerging contaminants for copper smelting exposure populations, providing valuable insights for pollution control in non-ferrous metal smelting. (c) 2024 The Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences. Published by Elsevier B.V.

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Glotzer, D. L.

A Cross-sectional Study on the Relationship Between a Metal Mixture and Oxidative Stress Biomarkers in Adolescents in Montevideo, Uruguay.

Thesis 2024

Introduction Exposure to heavy metals is toxic and associated with adverse health outcomes, particularly in children, and oxidative stress (OS) levels may be affected before overt signs are observed. Despite growing awareness that exposure to metals and other toxicants occurs in mixtures, often at low levels, this area of research remains significantly understudied, particularly among adolescents.

Objective We investigated the cross-sectional association between a metals mixture and urinary F2-isoprostanes (F2-isoPs) and 8-hydroxy- 2' -deoxyguanosine (8-OHdG) through the use of regression models and novel Bayesian Kernel Machine Regression methods (BKMR) to investigate potential nonlinear effects and interactions.

Methods : In this cross-sectional analysis, we obtained data from 421 adolescents participating in the Salud Ambiental Montevideo (SAM) cohort who were evaluated between July 2021 and August 2022. Fasting blood and spot urine samples were collected on the same day, together with anthropometry, and sociodemographic factors reported by caregivers. A suite of 20 metals were assessed via ICP-MS; F2-IsoP and 8-OHdG were measured using ELISA kits and their concentrations adjusted for specific gravity of urine. Biomarker values were log-transformed for analysis. Covariates were selected via directed acyclic graphs and review of the literature and included age, sex, socioeconomic status, Body Mass Index (BMI), presence of recent infections, secondhand smoke exposure, and physical activity.

Results : Together, 317 participants had complete data on all measures. These participants had a mean age of 12.0 +/- 2.2 years, 48.7% of whom are boys. Fifteen metals were above the limit of detection, including heavy metals like cadmium and lead and trace elements like copper and selenium. The median µg/L [IQR] for As, Cd, Pb, Mn, Co, and Cr was 0.4 [0.3-0.5], 0.1 [0.1-0.1], 1.2 [0.9-1.7], 9.6 [8.4-11.8], 0.3 [0.3-0.4], and 0.4 [0.3-0.4] respectively. The median pg/mL [IQR] for specific gravity adjusted F2-IsoP and 8-OHdG were 1769.9 [1216.6-2511.4] and 236.0146 234.0 [172.2-289.0] respectively. In the fully adjusted linear regression analysis, for F2-IsoP we found significant associations at an alpha of 0.05 for six predictors: Cu [β (95% CI)] = [-066. (-1.20.0, -0.13)] Mo [β (95% CI)] = [-0.20 (-0.39, -0.02)], Cs [β (95% CI)] = [-0.54 (-0.79, -0.29)], Cd [β (95% CI)] = [-0.17 (-0.28, -0.05)], V [β (95% CI)] = [-0.34 (-0.56, -0.12)], and Tl [β (95% CI)] = [-0.21 (-0.40, -0.02)]. For the outcome 8-OHdG only one predicator was significantly associated with the outcome with Ba having slightly positive relationship of [β (95% CI)] = [0.08 (0.00, 0.16)]. In BKMR analyses, a significant positive association was observed between the mixture and F2-IsoP at lower exposure levels, which became negative at higher exposure levels. In contrast, we found a non-significant inverse associations between the mixture and 8-OHdG.

Conclusion This study offers new insights into complex mixtures and their impacts on human development, while also advancing the exposomic approach to understanding environmental exposures.

https://www.webofscience.com/wos/pqdt/full-record/PQDT:89366985?SID=EUW1ED0DC8gm1o8AycmcPITITaoUg

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Wang, X., Zhang, Y., Peng, J., Zhang, H., Jiang, T., Zhang, Z.*, et al.*

Association Between Exposure to Multiple Toxic Metals in Follicular Fluid and the Risk of PCOS Among Infertile Women: The Mediating Effect of Metabolic Markers.

Biological Trace Element Research 2024.

Polycystic ovary syndrome (PCOS) severely affects women's fertility and accompanies serious metabolic disturbances, affecting 5%-20% of women of reproductive age globally. We previously found that exposure to toxic metals in the blood raised the risk of PCOS, but the association between

exposure to toxic metals and the risk of PCOS in the follicular fluid, the microenvironment for oocyte growth and development in females, and its effect on metabolism has not been reported. This study aimed to evaluate the associations between the concentrations of cadmium (Cd), mercury (Hg), barium (Ba) and arsenic (As) in FF and the risk of PCOS, and to explore the mediating effect of metabolic markers in FF on the above relationship.
We conducted a case-control study, including 557 women with PCOS and 651 controls. Ba, Cd, Hg and As levels in FF were measured by ICP-MS, metabolites levels in FF was measured by LC-MS/MS among 168 participants randomly selected from all the participants. Logistic regression models were used to assess the association of a single metal level with the PCOS risk, and linear regression models were used to assess the relationships of a single metal level with clinical phenotype parameters and metabolites levels. Combined effect of metals mixture levels on the risk of PCOS were assessed via weighted quantile sum (WQS) regression and bayesian kernel machine regression (BKMR). Medication analysis was performed to explore the role of metabolic markers on the relationship of toxic metals levels with the risk of PCOS. The exposure levels of Cd, Hg, Ba and As in FF were all positively and significantly associated with the PCOS risk (with respect to the highest vs. lowest tertile group: OR = 1.57, 95% CI = 1.17 similar to 2.12 for Cd, OR = 1.69, 95% CI = 1.22 similar to 2.34 for Hg, OR = 1.76, 95% CI = 1.32 similar to 2.34 for Ba, OR = 1.42, 95% CI = 1.05 similar to 1.91 for As). In addition, levels of metal mixture also significantly correlated with the risk of PCOS, Cd level contributed most to it. Moreover, we observed significant positive relationships between Cd level and LH (beta = 0.048, 95% CI = 0.002 similar to 0.094), T (beta = 0.077, 95% CI = 0.029 similar to 0.125) and HOMA-IR value (beta = 0.060, 95% CI = 0.012 similar to 0.107), as well as Hg level with LH, FSH/LH ratio and TC. Furthermore, we revealed that estrone sulfate, LysoPE 22:6 and N-Undecanoylglycine were significantly and positively mediating the association between Cd level and the risk of PCOS (with mediated proportion of 0.39, 0.24 and 0.35, respectively), and between Hg level and the risk of PCOS (with mediated proportion of 0.29, 0.20 and 0.46, respectively). These highly expressed metabolites significantly enriched in the fatty acid oxidation, steroid hormone biosynthesis and glycerophospholipids metabolism, which may explain the reason why the levels of Cd and Hg in FF associated with the phenotype of PCOS. Ba and As in FF was not found the above phenomenon. Our results suggested that exposure to multiple toxic metals (Cd, Hg, Ba and As) in FF associated with the increased risk of PCOS, Cd was a major contributor. Levels of Cd and Hg in FF significantly associated with the phenotype of PCOS. The above association may result from that Cd and Hg in FF related with the disturbance of fatty acid oxidation, steroid hormone biosynthesis and the glycerophospholipids metabolism.

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Yu, H., Chen, L., Chen, D., Gao, Y., Li, G., Shen, X.*, et al.*
Associations of multiple hydroxy-polycyclic aromatic hydrocarbons with serum levels of lipids in the workers from coking and non-ferrous smelting industries.
Journal of Hazardous Materials 2024; Vol. 473, p

Epidemiological evidence indicates that exposure to polycyclic aromatic hydrocarbons (PAHs) is associated with certain metabolic diseases. However, the relationship between PAHs and serum lipid profiles in exposed subjects remain unknown. Herein, the associations of multiple (8) urinary hydroxylated PAHs (OH-PAHs) in workers of coking (n = 655) and non-ferrous smelting (n = 614) industries with serum lipid levels (marking lipid metabolism) were examined. Multivariable linear regression, Bayesian kernel machine regression, and quantile g computation were used. Most urinary OH-PAHs were significantly higher ($p < 0.001$) in coking workers than in non-ferrous smelting workers. In workers of both industries, OH-PAH exposure was associated with elevated levels of serum total cholesterol, total triglyceride, and low -density lipoprotein, as well as reduced high -density lipoprotein levels. Specifically, urinary 4-hydroxyphenanthrene was significantly positively associated with serum total cholesterol, total triglyceride, and low -density lipoprotein levels in non-ferrous smelting workers;

however, the completely opposite association of 4-hydroxyphenanthrene with these lipid levels was observed in coking workers. The results of this pioneering examination suggest that exposure to OH-PAHs may contribute to dyslipidemia in coking and non-ferrous smelting workers, and distinct patterns of change were observed. Further prospective studies involving larger sample sizes are needed to further validate the findings.

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El Hajjar, M.
Etude des modifications du métabolisme des hydrocarbures aromatiques polycycliques en mélanges sur un modèle murin.
Université Grenoble Alpes 2023.
TIMC - Translational Innovation in Medicine and Complexity / Recherche Translationnelle et Innovation en Médecine et Complexité - UMR 5525

Les hydrocarbures aromatiques polycycliques (HAP) sont des polluants environnementaux produits en mélanges complexes dont la composition varie selon la source d'émission. Les HAP à haut poids moléculaires (HPM) sont classés comme cancérigènes probables ou possibles pour l'homme par le Centre International de Recherche sur le Cancer (CIRC) et le benzo[a]pyrène (B[a]P) est le seul HAP classé comme cancérigène certain. Pour exercer leur effet cancérigène, les HAP doivent être métabolisés. La biosurveillance de l'exposition aux HAP qui est très importante pour estimer les risques sanitaires des populations se fait par l'analyse des métabolites urinaires des HAP. Cependant, par manque de données épidémiologiques, il n'existe pas des valeurs toxicologiques de référence (VTR) pour ces polluants. D'où l'importance des modèles animaux pour fixer ces VTR. Ainsi la question qui se pose : Comment choisir le bon protocole animal pour étudier la toxicocinétique des HAP en mélange? Est-ce que les facteurs génétiques et environnementaux peuvent impacter les résultats de ces études? Pour répondre à ces questions et pouvoir extrapoler nos résultats à l'homme, 2 protocoles animaux ont été réalisés avec des expositions réalistes (faibles doses, mélange réel, exposition courte ou répétée). Le premier consistait à exposer par gavage des rats Sprague Dawley (SD) à de faibles doses (0,02 et 0,2 mg.kg-1.J-1) de B[a]P seul ou inclus dans un mélange industriel de HAP (ajusté à 0,2 mg.kg-1.J-1 de B[a]P) 5 fois.semaine-1 pendant 10 semaines. Le deuxième consistait à exposer par gavage des rats Wistar (W) au B[a]P seul (0,2 mg.kg-1.J-1) ou inclus dans un mélange industriel de HAP (ajusté à 0,2 mg.kg-1.J-1 de B[a]P) pendant 4 jours. En plus du dosage des métabolites urinaires du B[a]P et des HAP à HPM, nous avons mis au point l'analyse des HAP et/ou de leurs métabolites dans le sang, les fèces et les organes (foie et reins) par HPLC-Fluo et GC-MSMS-NCI après différents types d'extraction selon les matrices et les composés.
Aucune différence dans la toxicocinétique du B[a]P n'a été trouvée avec les deux doses utilisées. L'effet mélange ou l'effet cocktail était : augmentation de l'absorption du B[a]P, modification du métabolisme intestinal avec augmentation de la voie de bio-activation, diminution du métabolisme hépatique suite à une saturation/compétition enzymatique. L'effet de l'exposition répétée pendant 10 semaines était : augmentation de l'absorption des HAP après exposition au B[a]P et au mélange de HAP sans modification du métabolisme intestinal, augmentation du métabolisme hépatique uniquement après exposition au B[a]P seul à faible dose (0,02 mg.kg-1.J-1). La variabilité inter-souche entre les SD et les W a montré que l'absorption et le métabolisme intestinal du fluoranthène et du pyrène étaient identiques entre les 2 souches. Cependant, l'absorption des HAP à HPM était plus faible chez les SD avec un métabolisme intestinal du B[a]P orienté vers la voie de bio-activation. Le métabolisme hépatique était plus élevé chez les SD. Une grande variabilité inter-individuelle était observée entre les rats W exposés au mélange de HAP au niveau de l'absorption intestinale des HAP à HPM et de leur métabolisme hépatique. Il existait des profils différents de formation des métabolites au niveau hépatique alors que le métabolisme intestinal était comparable entre les rats.Le jeûne augmentait l'absorption du B[a]P mais le métabolisme intestinal et hépatique étaient diminués et/ou modifiés

avec une augmentation de la voie de bio-activation.Ce travail contribue à la réflexion sur le choix du modèle animal et des conditions d'exposition pour la détermination des VTR et l'évaluation des risques des populations dans un contexte de poly-expositions qui est beaucoup plus complexe qu'un simple effet additif.

https://theses.hal.science/tel-04188578

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Multi-expositions aux particules de microplastiques, pesticides

GODINEZ-PEREZ B.M. ; SCHILMANN A.; LAGUNAS-MARTINEZ A.; ESCAMILLA-NUNEZ C.; ET COLL.
Pesticide use patterns and their association with cytokine levels in Mexican flower workers. (Modèles d'utilisation des pesticides et leur association avec les niveaux de cytokines chez les fleuristes mexicains).
International Archives of Occupational and Environmental Health, n° 3, vol. 97, avril 2024, pp. 291-302, ill., bibliogr. (En anglais)
Cet article examine l'association entre l'exposition aux pesticides et les niveaux de cytokines chez les cultivateurs de fleurs au Mexique. Les travailleurs des fleurs exposés à certains schémas d'utilisation de pesticides ont montré des concentrations élevées de cytokines pro-inflammatoires IL-6 et IFN-gamma, suggérant une association entre l'exposition aux pesticides et des effets sur la réponse immunitaire. L'étude a été menée chez 108 travailleurs de la floriculture et les niveaux de certaines interleukines ont été mesurés pour établir le lien entre une réaction inflammatoire et l'exposition à différents schémas d'utilisation des pesticides. L'analyse a révélé que certains modes d'utilisation des pesticides, combinant insecticides et fongicides, étaient associés à des niveaux plus élevés de cytokines pro-inflammatoires. Ces résultats indiquent que les pesticides peuvent avoir des propriétés immunotoxiques, contribuant à une augmentation de la réponse inflammatoire. Toutefois, d'autres études épidémiologiques approfondies sont nécessaires pour établir une relation de cause à effet.

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Alijagic, A., Suljevic, D., Focak, M., Sulejmanovic, J., Sehovic, E., Sarndahl, E., Engwall, M.
The triple exposure nexus of microplastic particles, plastic-associated chemicals, and environmental pollutants from a human health perspective.
Environment international 2024; Vol. 188, p 108736-108736.

The presence of microplastics (MPs) is increasing at a dramatic rate globally, posing risks for exposure and subsequent potential adverse effects on human health. Apart from being physical objects, MP particles contain thousands of plastic-associated chemicals (i.e., monomers, chemical additives, and non-intentionally added substances) captured within the polymer matrix. These chemicals are often migrating from MPs and can be found in various environmental matrices and human food chains; increasing the risks for exposure and health effects. In addition to the physical and chemical attributes of MPs, plastic surfaces effectively bind exogenous chemicals, including environmental pollutants (e.g., heavy metals, persistent organic pollutants). Therefore, MPs can act as vectors of environmental pollution across air, drinking water, and food, further amplifying health risks posed by MP exposure. Critically, fragmentation of plastics in the environment increases the risk for interactions with cells,

increases the presence of available surfaces to leach plastic-associated chemicals, and adsorb and transfer environmental pollutants. Hence, this review proposes the so-called triple exposure nexus approach to comprehensively map existing knowledge on interconnected health effects of MP particles, plastic-associated chemicals, and environmental pollutants. Based on the available data, there is a large knowledge gap in regard to the interactions and cumulative health effects of the triple exposure nexus. Each component of the triple nexus is known to induce genotoxicity, inflammation, and endocrine disruption, but knowledge about long-term and inter-individual health effects is lacking. Furthermore, MPs are not readily excreted from organisms after ingestion and they have been found accumulated in human blood, cardiac tissue, placenta, etc. Even though the number of studies on MPs-associated health impacts is increasing rapidly, this review underscores that there is a pressing necessity to achieve an integrated assessment of MPs' effects on human health in order to address existing and future knowledge gaps.

https://doi.org/10.1016/j.envint.2024.108736

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Sudarsan, J. S., Dogra, K., Kumar, R., Raval, N. P., Leifels, M., Mukherjee, S.*, et al.*
Tricks and tracks of prevalence, occurrences, treatment technologies, and challenges of mixtures of emerging contaminants in the environment: With special emphasis on microplastic.
Journal of Contaminant Hydrology 2024; Vol. 265, p 104389.

This paper aims to emphasize the occurrence of various emerging contaminant (EC) mixtures in natural ecosystems and highlights the primary concern arising from the unregulated release into soil and water, along with their impacts on human health. Emerging contaminant mixtures, including pharmaceuticals, personal care products, dioxins, polychlorinated biphenyls, pesticides, antibiotics, biocides, surfactants, phthalates, enteric viruses, and microplastics (MPs), are considered toxic contaminants with grave implications. MPs play a crucial role in transporting pollutants to aquatic and terrestrial ecosystems as they interact with the various components of the soil and water environments. This review summarizes that major emerging contaminants (ECs), like trimethoprim, diclofenac, sulfamethoxazole, and 17α-Ethinylestradiol, pose serious threats to public health and contribute to antimicrobial resistance. In addressing human health concerns and remediation techniques, this review critically evaluates conventional methods for removing ECs from complex matrices. The diverse physiochemical properties of surrounding environments facilitate the partitioning of ECs into sediments and other organic phases, resulting in carcinogenic, teratogenic, and estrogenic effects through active catalytic interactions and mechanisms mediated by aryl hydrocarbon receptors. The proactive toxicity of ECs mixture complexation and, in part, the yet-to-be-identified environmental mixtures of ECs represent a blind spot in current literature, necessitating conceptual frameworks for assessing the toxicity and risks with individual components and mixtures. Lastly, this review concludes with an in-depth exploration of future scopes, knowledge gaps, and challenges, emphasizing the need for a concerted effort in managing ECs and other organic pollutants.

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Guo, J., Garshick, E., Si, F., Tang, Z., Lian, X., Wang, Y.*, et al.*
Environmental Toxicant Exposure and Depressive Symptoms.
JAMA Network Open 2024; Vol. 7 (7), p e2420259.

Recognizing associations between exposure to common environmental toxicants and mental disorders such as depression is crucial for guiding targeted mechanism research and the initiation of disease prevention efforts. To comprehensively screen and assess the associations between potential

environmental toxicants and depressive symptoms and to assess whether systemic inflammation serves as a mediator. A total of 3427 participants from the 2013-2014 and 2015-2016 waves of the National Health and Nutrition Examination and Survey who had information on blood or urine concentrations of environmental toxicants and depression scores assessed by the 9-item Patient Health Questionnaire (PHQ-9) were included. Statistical analysis was performed from July 1, 2023, to January 31, 2024.Sixty-two toxicants in 10 categories included acrylamide, arsenic, ethylene oxide, formaldehyde, iodine, metals, nicotine metabolites, polycyclic aromatic hydrocarbons, volatile organic compound (VOC) metabolites; and perchlorate, nitrate, and thiocyanate. An exposome-wide association study and the deletion-substitution-addition algorithm were used to assess associations with depression scores (PHQ-9 ≥5) adjusted for other important covariates. A mediation analysis framework was used to evaluate the mediating role of systemic inflammation assessed by the peripheral white blood cell count. Among the 3427 adults included, 1735 (50.6%) were women, 2683 (78.3%) were younger than 65 years, and 744 (21.7%) were 65 years or older, with 839 (24.5%) having depressive symptoms. In terms of race and ethnicity, 570 participants (16.6%) were Mexican American, 679 (19.8%) were non-Hispanic Black, and 1314 (38.3%) were non-Hispanic White. We identified associations between 27 chemical compounds or metals in 6 of 10 categories of environmental toxicants and the prevalence of depressive symptoms, including the VOC metabolites N-acetyl-S-(2-hydroxy-3-butenyl)-l-cysteine (odds ratio [OR], 1.74 [95% CI, 1.38, 2.18]) and total nicotine equivalent-2 (OR, 1.42 [95% CI, 1.26-1.59]). Men and younger individuals appear more vulnerable to environmental toxicants than women and older individuals. Peripheral white blood cell count mediated 5% to 19% of the associations. In this representative cross-sectional study of adults with environmental toxicant exposures, 6 categories of environmental toxicants were associated with depressive symptoms with mediation by systemic inflammation. This research provides insight into selecting environmental targets for mechanistic research into the causes of depression and facilitating efforts to reduce environmental exposures.

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Udovicki, B., Tomic, N., Brkic, D., Sredojevic, A., Kaludjerovic, M., Trifunovic, B. S.*, et al.*
Cumulative risk assessment of dietary exposure of the adult population in Serbia to pesticides that have chronic effects on the thyroid gland through fresh fruits and vegetables.
Food and Chemical Toxicology 2024; Vol. 186, p

In contrast to the traditional approach to risk assessment, which focuses on a single chemical, cumulative exposure and risk assessment considers the consequences of exposure to multiple chemical combinations. A cumulative risk assessment of dietary exposure of adult females and adult males to pesticides with chronic effects on the thyroid was conducted by estimation of the Total Margin of Exposure (MOET). Exposure to each active substance was estimated using a second-order Monte Carlo simulation. Input values for the simulation were based on over 2300 conventionally produced fruit and vegetable samples analysed from 2021 to 2023 and consumption data collected using the Food Frequency Questionnaire (FFQ) and 24h recall method. MOET values, for both populations assessed, did not exceed thresholds for regulatory consideration established by risk managers. Considering that MOETs values from consumption of fresh fruits and vegetables were relatively close to the threshold value, total exposure to the pesticides could likely reach risk-associated MOET levels, through the consumption of other food products that may be contaminated.

https://doi.org/10.1016/j.fct.2024.114541

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Li, H., Lin, L., Liu, H., Deng, X., Wang, L., Kuang, Y.*, et al.*
Simultaneous exposure to nanoplastics and cadmium mitigates microalgae cellular toxicity: Insights from molecular simulation and metabolomics.
Environment International 2024; Vol. 186

In the severe pollution area of nanoplastics (NPs) and cadmium ions (Cd 2+), the joint effects of their high environmental concentrations on primary producers may differ from those of low environmental doses. Thus, we investigated the physiological changes, cell morphology, molecular dynamic simulation, phenotypic interactions, and metabolomics responses of C. pyrenoidosa to high environmental concentrations of NPs and Cd 2+ after 12d acclimation. After 12-d cultivation, mono-NPs and mono-Cd2+ reduced cell density and triggered antioxidant enzymes, extracellular polymeric substances (EPS) production, and cell aggregation to defend their unfavorable effects. Based on the molecular dynamic simulation, the chlorine atoms of the NPs and Cd 2+ had charge attraction with the nitrogen and phosphorus atoms in the choline and phosphate groups in the cell membrane, thereby NPs and Cd 2 + could adsorb on the cells to destroy them. In the joint exposure, NPs dominated the variations of ultrastructure and metabolomics and alleviated the toxicity of NPs and Cd 2 +. Due to its high environmental concentration, more NPs could compete with the microalgae for Cd 2 + and thicken cell walls, diminishing the Cd 2 + content and antioxidant enzymes of microalgae. NPs addition also decreased the EPS content, while the bound EPS with -CN bond was kept to detoxicate Cd 2 +. Metabolomics results showed that the NPs downregulated nucleotide, arachidonic acid, and tryptophan metabolisms, while the Cd 2 + showed an opposite trend. Compared with their respective exposures, metabolomics results found the changes in metabolic molecules, suggesting the NPs_Cd 2 + toxicity was mitigated by balancing nucleotide, arachidonic acid, tryptophan, and arginine and proline metabolisms. Consequently, this study provided new insights that simultaneous exposure to high environmental concentrations of NPs and Cd 2 + mitigated microalgae cellular toxicity, which may change their fates and biogeochemical cycles in aquatic systems.

https://doi.org/10.1016/j.envint.2024.108633

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Assadi, S. N.
Cardiovascular disorders and exposure to chemical pollutants.
Journal of preventive medicine and hygiene 2024; Vol. 65 (1), p E59-E64.

Introduction: Exposure with some chemical can cause cardiovascular disorders. Occupational exposures with chemicals are modifiable risk factors for cardiovascular diseases. The Objective of this study was the determination of cardiovascular disorders in industries with occupational exposures.
Materials and methods: Study was a cross-sectional method and was done on workers of related industries. The study was done with a physical examination and checklist by getting health and illness history and clinical tests about the risk factors and cardiovascular disorders. According to exposures the population of the study was divided into 3 groups. Data were analyzed with SPSS 16, by considering $p < 0.05$ as significant.
Results: The frequency of unstable angina and stable angina were the most in group 1. The relative risk for unstable angina was 1.55 (1.46-1.61) in group 1 and for stable angina was 1.54 (1.47-1.62) in this group. The risk of thrombophlebitis was 8.48 (7.07-10.17) in group 2.
Conclusions: Workers in industry with chemical pollutants had cardiovascular disorders. The occupational exposures, especially chemical agents are effective on cardiovascular system.

https://doi.org/10.15167/2421-4248/jpmh2024.65.1.3126

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Mahoney, H., Da Silva, F., Brinkmann, M., Giesy, J. P.
Mixtures of legacy and replacement perfluorosulphonic acids (PFSAs) demonstrate ratio-, concentration- and endpoint-dependent synergistic interactions in vitro.
Chemosphere 2024; Vol. 361, p 142446.

The extensive use of poly- and per-fluoroalkyl substances (PFASs) has les to their widespread presence in the environment, raising concerns about potential toxicity. While certain PFASs of concern have been phased-out or banned, new PFASs continue to be produced. Two such substances are perfluoroethylcyclohexane sulphonate (PFECHS) and perfluorobutane sulphamide (FBSA), replacements of perfluoroctanesulphonic acid (PFOS) that have recently been detected in multiple environmental media around the globe. Despite PFASs generally occurring in the environment as mixtures, few data are available outlining the effects of PFAS mixtures. Therefore, this research investigated the interaction potential of binary and ternary mixtures of emerging and legacy PFASs. The immortalized rainbow trout gill cell line (RTgill-W1) was chosen as the experimental model to investigate two apical endpoints: cytotoxicity and phospholipidosis. RTgill-W1 cells were exposed for 24h to each compound to obtain endpoint-specific effect concentrations (LCx; ECx). These values were then applied to formulate mixture predictions following the Loewes Additivity and Steel and Peckham methods. Based on cytotoxicity, relative potencies of individual compounds were: PFOS>PFECHS>FSBA. PFOS and PFECHS had nearly identical effects on phospholipidosis, while FSBA did not have any effects. Most mixtures had a synergistic effect on cytotoxicity, but the effect was both dose- and ratio-dependent. PFOS and PFECHS were additive at lower concentrations (LC10) and synergistic at higher concentrations (LC50; 3:1, 1:1, and 1:3). PFECHS and FSBA mixtures were synergistic at all doses and ratios (3:1, 1:1, 1:3), while FBSA and PFOS were mainly synergistic at higher concentrations and at ratios favouring PFOS (1:1, 1:3). Tertiary combinations were mainly synergistic. For phospholipidosis, mixtures were strictly additive. These results are strongly suggestive of synergism between emerging PFAS replacements and highlight that independent apical mechanisms of different PFASs could combine to induce unexpected toxicity. Considering that emerging replacements are continuing to increase in concentration in the environment, such mixture scenarios are also likely to continue to increase in probability.

https://doi.org/10.1016/j.chemosphere.2024.142446

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Fuhrimann, S., Mueller, W., Atuhaire, A., Mubeezi, R., Ohlander, J., Povey, A.*, et al.*
Occupational exposure to pesticides and neurobehavioral outcomes. Impact of different original and recalled exposure measures on the associations.
Annals of Work Exposures and Health 2024; Vol.

Several measures of occupational exposure to pesticides have been used to study associations between exposure to pesticides and neurobehavioral outcomes. This study assessed the impact of different exposure measures for glyphosate and mancozeb on the association with neurobehavioral outcomes based on original and recalled self-reported data with 246 smallholder farmers in Uganda. The association between the 6 exposure measures and 6 selected neurobehavioral test scores was investigated using linear multivariable regression models. Exposure measures included original exposure measures for the previous year in 2017: (i) application status (yes/no), (ii) number of application days, (iii) average exposure-intensity scores (EIS) of an application and (iv) number of EIS-weighted application days. Two additional measures were collected in 2019: (v) recalled application status and (vi) recalled EIS for the respective periods in 2017.Recalled applicator status and EIS were between 1.2 and 1.4 times more frequent and higher for both pesticides than the original application status and EIS. Adverse associations between the different original measures of exposure to glyphosate and 4 neurobehavioral tests were observed. Glyphosate exposure based on recalled information and all mancozeb exposure measures were not associated with the neurobehavioral outcomes. The

relation between the different original self-reported glyphosate exposure measures and neurobehavioral test scores appeared to be robust. When based on recalled exposure measures, associations observed with the original exposure measures were no longer present. Therefore, future epidemiological studies on self-reported exposure should critically evaluate the potential bias towards the null in observed exposure–response associations.

https://doi.org/10.1093/annweh/wxae025

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Expositions multiples aux polluants ambiants, VOCs

Ricklund N. ; Bryngelsson I.L.; Hagberg J.
Occupational exposure to volatile organic compounds (VOCs), including aldehydes for Swedish hairdressers. (Exposition professionnelle aux composés organiques volatils (COV), y compris les aldéhydes, chez des coiffeurs suédois).
Annals of Work Exposures and Health, n° 3, vol. 67, avril 2023, pp. 366-378 (En anglais)

Dans cette étude, l'exposition aux composés organiques volatils (COV), y compris les aldéhydes, a été mesurée dans la zone de respiration individuelle de 30 coiffeurs répartis uniformément dans dix salons de coiffure de la ville d'Örebro, en Suède. Les tâches réalisées et l'air intérieur ont également été surveillés. Un indice de danger (IH) basé sur des valeurs de référence chroniques pour la santé a été calculé pour indiquer le risque d'exposition combiné. Au total, 90 COV, dont neuf aldéhydes, ont été identifiés. L'exposition individuelle exprimée en concentration totale de COV était comprise entre 50 et 3 600 µg/m3 d'équivalent toluène et les valeurs de l'IH allaient de 0,0046 à 13. Les méthodes de travail individuelles, la ventilation, l'utilisation volumétrique des produits de traitement capillaire, certaines substances chimiques contenues dans les produits (formaldéhyde, isopropanol et diisocyanate de 2,4 et 2,6-toluène) et la disponibilité de valeurs de référence ont pu affecter les estimations des risques d'exposition. Néanmoins, l'IH peut servir d'outil de dépistage pour évaluer le risque d'exposition potentiel des coiffeurs, car il tient compte de la complexité des mélanges chimiques et de la composante chronique de l'exposition aux COV dans tous les environnements intérieurs.
Références INRS-Biblio : 731010

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Han, S., Xie, M., Cheng, S., Han, Y., Li, P., Guo, J.
Associations between specific volatile organic chemical exposures and cardiovascular disease risks: insights from NHANES.
Frontiers in public health 2024; Vol. 12 p 1378444.

Introduction: An increasing body of research has demonstrated a correlation between pollutants from the environment and the development of cardiovascular diseases (CVD). However, the impact of volatile organic chemicals (VOC) on CVD remains unknown and needs further investigation.
Objectives: This study assessed whether exposure to VOC was associated with CVD in the general population. Methods: A cross-sectional analysis was conducted utilizing data from five survey cycles (2005-2006, 2011-2012, 2013-2014, 2015-2016, and 2017-2018) of the National Health and Nutrition Examination Survey (NHANES) program. We analyzed the association between urinary VOC

metabolites (VOCs) and participants by multiple logistic regression models, further Bayesian Kernel Machine Regression (BKMR) models and Weighted Quantile Sum (WQS) regression were performed for mixture exposure analysis.
Results: Total VOCs were found to be positively linked with CVD in multivariable-adjusted models (p for trend=0.025), independent of established CVD risk variables, such as hypertension, diabetes, drinking and smoking, and total cholesterol levels. Compared with the reference quartile of total VOCs levels, the multivariable-adjusted odds ratios in increasing quartiles were 1.01 [95% confidence interval (CI): 0.78-1.31], 1.26 (95% CI: 1.05-1.21) and 1.75 (95% CI: 1.36-1.64) for total CVD. Similar positive associations were found when considering individual VOCs, including AAMA, CEMA, CYMA, 2HPMA, 3HPMA, IPM3 and MHBMA3 (acrolein, acrylamide, acrylonitrile, propylene oxide, isoprene, and 1,3-butadiene). In BKMR analysis, the overall effect of a mixture is significantly related to VOCs when all chemicals reach or exceed the 75th percentile. Moreover, in the WQS models, the most influential VOCs were found to be CEMA (40.30%), DHBMA (21.00%), and AMCC (19.70%).
Conclusion: The results of our study indicated that VOC was all found to have a significant association with CVD when comparing results from different models. These findings hold significant potential for public health implications and offer valuable insights for future research directions.

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Uttajug, A., Seposo, X., Phosri, A., Phung, V. L. H., Tajudin, M. a. B. A., Ueda, K.
Effects of Coexposure to Air Pollution from Vegetation Fires and Extreme Heat on Mortality in Upper Northern Thailand.
Environmental science & technology 2024; Vol. 58 (23) p 9945-9953.

Background: understanding the effects of coexposure to compound extreme events, such as air pollution and extreme heat, is important for reducing current and future health burdens. This study investigated the independent and synergistic effects of exposure to air pollution from vegetation fires and extreme heat on all-cause mortality in Upper Northern Thailand. Methods: we used a time-stratified case-crossover study design with a conditional quasi-Poisson model to examine the association between mortality and coexposure to air pollution due to vegetation fire events (fire-PM2.5) and extreme heat. Extreme heat days were defined using the 90th and 99th percentile thresholds for daily maximum temperature.
Results: we observed a significant positive excess risk of mortality due to independent exposure to fire-PM2.5 and extreme heat, but not an interactive effect. All-cause mortality risk increased by 0.9% (95% confidence interval (CI): 0.1, 1.8) for each 10 mug/m3 increase in fire-PM2.5 on the same day and by 12.8% (95% CI: 10.5, 15.1) on extreme heat days (90th percentile) relative to nonextreme heat days.
Conclusion: this study showed that exposure to PM2.5 from vegetation fires and extreme heat independently increased all-cause mortality risk in UNT. However, there was no evidence of a synergistic effect of these events.

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Liu, W., Ye, L., Hua, B., Yang, Y., Dong, Z., Jiang, Y.*, et al.*
Association between combined exposure to ambient air pollutants, genetic risk, and incident gout risk: A prospective cohort study in the UK Biobank.
Seminars in Arthritis and Rheumatism 2024; Vol. 66, 152445.

Background: Limited research has been conducted on the association between long-term exposure to air pollutants and the incidence of gout.

Objectives: This study aims to assess the individual and combined effects of prolonged exposure to five air pollutants (NO2, NOx, PM10, PMcoarse and PM2.52) on the incidence of gout among 458,884 initially gout-free participants enrolled in the UK Biobank.
Methods: Employing a land use regression model, we utilized an estimation method to ascertain the annual concentrations of the five air pollutants. Subsequently, we devised a weighted air pollution score to facilitate a comprehensive evaluation of exposure. The Cox proportional hazards model was utilized to investigate the association between ambient air pollution and gout risk. Interaction and stratification analyses were conducted to evaluate age, sex, BMI, and genetic predisposition as potential effect modifiers in the air pollution-gout relationship. Furthermore, mediation analyses were conducted to explore the potential involvement of biomarkers in mediating the association between air pollution and gout.
Results: Over a median follow-up time of 12.0 years, 7,927 cases of gout were diagnosed. Significant associations were observed between the risk of gout and a per IQR increase in NO2 (HR3: 1.05, 95 % CI4: 1.02-1.08, p = 0.003), NOx (HR: 1.04, 95 % CI: 1.01-1.06, p = 0.003), and PM2.5 (HR: 1.03, 95 % CI: 1.00-1.06, p = 0.030). Per IQR increase in the air pollution score was associated with an elevated risk of gout (p = 0.005). Stratified analysis revealed a significant correlation between the air pollution score and gout risk in participants >= 60 years (HR: 1.05, 95 % CI: 1.02-1.09, p = 0.005), but not in those <60 years (p = 0.793), indicating a significant interaction effect with age (p-interaction=0.009). Mediation analyses identified five serum biomarkers (SUA:15.87 %, VITD: 5.04 %, LDLD: 3.34 %, GGT: 1.90 %, AST: 1.56 %(5)) with potential mediation effects on this association.
Conclusions: Long-term exposure to air pollutants, particularly among the elderly population, is associated with an increased risk of gout. The underlying mechanisms of these associations may involve the participation of five serum biomarkers.

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Antonelli, J., Zigler, C. M.
Causal Analysis of Air Pollution Mixtures: Estimands, Positivity, and Extrapolation.
American journal of epidemiology 13 june 2024; Vol., p

Causal inference for air pollution mixtures is an increasingly important issue with appreciable challenges. When the exposure is a multivariate mixture, there are many exposure contrasts that may be of nominal interest for causal effect estimation, but the complex joint mixture distribution often renders observed data extremely limited in their ability to inform estimates of many commonly-defined causal effects. We use potential outcomes to 1) define causal effects of air pollution mixtures, 2) formalize the key assumption of mixture positivity required for estimation and 3) offer diagnostic metrics for positivity violations in the mixture setting that allow researchers to assess the extent to which data can actually support estimation of mixture effects of interest. For settings where there is limited empirical support, we redefine causal estimands that apportion causal effects according to whether they can be directly informed by observed data versus rely entirely on model extrapolation, isolating key sources of information on the causal effect of an air pollution mixture. The ideas are deployed to assess the ability of a national United States data set on the chemical components of ambient particulate matter air pollution to support estimation of a variety of causal mixture effects.

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Amadou, A., Giampiccolo, C., Ngaleu, F. B., Praud, D., Coudon, T., Grassot, L.*, et al.*
Multiple xenoestrogen air pollutants and breast cancer risk: Statistical approaches to investigate combined exposures effect.
Environmental Pollution ; 15 june 2024; Vol. 351, 124043

Studies suggested that exposure to air pollutants, with endocrine disrupting (ED) properties, have a key role in breast cancer (BC) development. Although the population is exposed simultaneously to a mixture of multiple pollutants and ED pollutants may act via common biological mechanisms leading to synergic effects, epidemiological studies generally evaluate the effect of each pollutant separately. We aimed to assess the complex effect of exposure to a mixture of four xenoestrogen air pollutants (benzo-[a]-pyrene (BaP), cadmium, dioxin (2,3,7,8Te<acute accent>trachlorodibenzo-p-dioxin TCDD)), and polychlorinated biphenyl 153 (PCB153)) on the risk of BC, using three recent statistical methods, namely weighted quantile sum (WQS), quantile g -computation (QGC) and Bayesian kernel machine regression (BKMR). The study was conducted on 5222 cases and 5222 matched controls nested within the French prospective E3N cohort initiated in 1990. Annual average exposure estimates to the pollutants were assessed using a chemistry transport model, at the participants' residence address between 1990 and 2011. We found a positive association between the WQS index of the joint effect and the risk of overall BC (adjusted odds ratio (OR) = 1.10, 95% confidence intervals (CI): 1.03-1.19). Similar results were found for QGC (OR = 1.11, 95%CI: 1.03-1.19). Despite the association did not reach statistical significance in the BKMR model, we observed an increasing trend between the joint effect of the four pollutants and the risk of BC, when fixing other chemicals at their median concentrations. BaP, cadmium and PCB153 also showed positive trends in the multipollutant mixture, while dioxin showed a modest inverse trend. Despite we found a clear evidence of a positive association between the joint exposure to pollutants and BC risk only from WQS and QGC regression, we observed a similar suggestive trend using BKMR. This study makes a major contribution to the understanding of the joint effects of air pollution.

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Zhang, S., Tang, H., Zhou, M., Pan, L.
Sexual dimorphism association of combined exposure to volatile organic compounds (VOC) with kidney damage.
Environmental Research 2024; Vol. 258, p 119426.

Background Epidemiological evidence emphasizes air pollutants' role in chronic kidney disease (CKD). Volatile organic compounds (VOCs) contribute to air pollution, yet research on VOCs and kidney damage, especially gender disparities, is limited.
Methods This study analyzed NHANES data to explore associations between urinary VOC metabolite mixtures (VOCMs) and key kidney-related parameters: estimated glomerular filtration rate (eGFR), albumin-to-creatinine ratio (ACR), chronic kidney disease (CKD), and albuminuria. Mediation analyses assessed the potential mediating roles of biological aging (BA) and serum albumin in VOCM mixtures' effects on kidney damage. Sensitivity analyses were also conducted.
Results The mixture analysis unveiled a noteworthy positive association between VOCM mixtures and the risk of developing CKD, coupled with a significant negative correlation with eGFR within the overall participant cohort. These findings remained consistent when examining the female subgroup. However, among male participants, no significant link emerged between VOCM mixtures and CKD or eGFR. Furthermore, in both the overall and female participant groups, there was an absence of a significant correlation between VOCM mixtures and either ACR or albuminuria. On the other hand, in male participants, while no significant correlation was detected with albuminuria, a significant positive correlation was observed with ACR. Pollutant analysis identified potential links between kidney damage and 1,3-butadiene, toluene, ethylbenzene, styrene, xylene, acrolein, crotonaldehyde and

propylene oxide. Mediation analyses suggested that BA might partially mediate the relationship between VOCM mixtures and kidney damage.
Conclusion The current findings highlight the widespread exposure to VOCs among the general U.S. adult population and indicate a potential correlation between exposure to VOC mixtures and compromised renal function parameters, with notable gender disparities. Females appear to exhibit greater sensitivity to impaired renal function resulting from VOCs exposure. Anti-aging treatments may offer some mitigation against kidney damage due to VOCs exposure.

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Traini, E., Portengen, L., Ohanyan, H., Van Vorstenbosch, R., Vermeulen, R., Huss, A.
A prospective exploration of the urban exposome in relation to headache in the Dutch population-based Occupational and environmental health cohort study (AMIGO).
Environment international 2024; Vol. 188 p 108776.

OBJECTIVE: Headache is one of the most prevalent and disabling health conditions globally. We prospectively explored the urban exposome in relation to weekly occurrence of headache episodes using data from the Dutch population-based Occupational and Environmental Health Cohort Study (AMIGO).
MATERIAL AND METHODS: Participants (N=7,339) completed baseline and follow-up questionnaires in 2011 and 2015, reporting headache frequency. Information on the urban exposome covered 80 exposures across 10 domains, such as air pollution, electromagnetic fields, and lifestyle and socio-demographic characteristics. We first identified all relevant exposures using the Boruta algorithm and then, for each exposure separately, we estimated the average treatment effect (ATE) and related standard error (SE) by training causal forests adjusted for age, depression diagnosis, painkiller use, general health indicator, sleep disturbance index and weekly occurrence of headache episodes at baseline. RESULTS: Occurrence of weekly headache was 12.5% at baseline and 11.1% at follow-up. Boruta selected five air pollutants (NO2, NOX, PM10, silicon in PM10, iron in PM2.5) and one urban temperature measure (heat island effect) as factors contributing to the occurrence of weekly headache episodes at follow-up. The estimated causal effect of each exposure on weekly headache indicated positive associations. NO2 showed the largest effect (ATE=0.007 per interquartile range (IQR) increase; SE=0.004), followed by PM10 (ATE=0.006 per IQR increase; SE=0.004), heat island effect (ATE=0.006 per one-degree Celsius increase; SE=0.007), NOx (ATE=0.004 per IQR increase; SE=0.004), iron in PM2.5 (ATE=0.003 per IQR increase; SE=0.004), and silicon in PM10 (ATE=0.003 per IQR increase; SE=0.004). CONCLUSION: Our results suggested that exposure to air pollution and heat island effects contributed to the reporting of weekly headache episodes in the study population.

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Saucy, A., Ortega, N., Tonne, C.
Residential relocation to assess impact of changes in the living environment on cardio-respiratory health: A narrative literature review with considerations for exposome research.
Environmental research 2024; Vol. 244 p 117890.

Residential relocation studies have become increasingly valuable tools for evaluating the effects of changing living environments on human health, but little is known about their application to multiple aspects of the living environment and the most appropriate methodology. This narrative review explores the utility of residential relocation as a natural experiment for studying the impact of changing

urban exposures on cardio-metabolic health in high-income settings. It provides a comprehensive overview of the use of residential relocation studies, evaluates their methodological approaches, and synthesizes findings related to health behaviors and cardio-metabolic outcomes. Our search identified 43 relevant studies published between January 1995 and February 2023, from eight countries, predominantly the USA, Canada, and Australia. The majority of eligible studies were published between 2012 and 2021 and examined changes in various domains of the living environment, such as walkability, the built and social environments, but rarely combinations of exposures. Included studies displayed heterogeneity in design and outcomes, 25 involving only movers and 18 considering both movers and non-movers. To mitigate the issue of residential self-selection bias, most studies employed a "change-in-change" design and adjusted for baseline covariates but only a fraction of them accounted for time-varying confounding. Relocation causes simultaneous changes in various features of the living environment, which presents an opportunity for exposome research to establish causal relationships, using large datasets with increased statistical power and a wide range of health outcomes, behaviors and biomarkers. Residential relocation is not a random process. Thus, studies focusing on living environment characteristics need to carefully select time-varying covariates and reference group. Overall, this review informs future research by guiding choices in study design, data requirements, and statistical methodologies. Ultimately, it contributes to the advancement of the urban exposome field and enhances our understanding of the complex relationship between urban environments and human health.

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Liu, X., Chang, Y., Xu, C., Li, Y., Wang, Y., Sun, Y.*, et al.*
Association of volatile organic compound levels with chronic obstructive pulmonary diseases in NHANES 2013–2016.
Scientific Reports 2024; Vol. 14 (1) p 16085.

Volatile organic compounds (VOCs) represent a significant component of air pollution. However, studies evaluating the impact of VOC exposure on chronic obstructive pulmonary disease (COPD) have predominantly focused on single pollutant models. This study aims to comprehensively assess the relationship between multiple VOC exposures and COPD. A large cross-sectional study was conducted on 4983 participants from the National Health and Nutrition Examination Survey. Four models, including weighted logistic regression, restricted cubic splines (RCS), weighted quantile sum regression (WQS), and the dual-pollution model, were used to explore the association between blood VOC levels and the prevalence of COPD in the U.S. general population. Additionally, six machine learning algorithms were employed to develop a predictive model for COPD risk, with the model's predictive capacity assessed using the area under the curve (AUC) indices. Elevated blood concentrations of benzene, toluene, ortho-xylene, and para-xylene were significantly associated with the incidence of COPD. RCS analysis further revealed a non-linear and non-monotonic relationship between blood levels of toluene and m-p-xylene with COPD prevalence. WQS regression indicated that different VOCs had varying effects on COPD, with benzene and ortho-xylene having the greatest weights. Among the six models, the Extreme Gradient Boosting (XGBoost) model demonstrated the strongest predictive power, with an AUC value of 0.781. Increased blood concentrations of benzene and toluene are significantly correlated with a higher prevalence of COPD in the U.S. population, demonstrating a non-linear relationship. Exposure to environmental VOCs may represent a new risk factor in the etiology of COPD.

https://doi.org/10.1038/s41598-024-67210-7

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