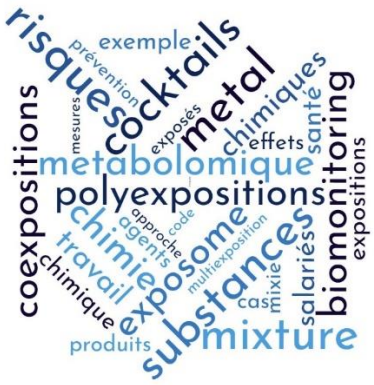

Bulletin de veille
Polyexpositions chimiques
N°7 – janvier 2025

Objectif : la polyexposition homogène chimie/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 cette co-exposition à plusieurs composés chimiques.

Ce bulletin a été réalisé à partir d'une surveillance de littérature récente sur les bases Web of Sciences 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

- 27 novembre 2024. Expertise Anses. Pollution du trafic routier : des risques accrus pour les travailleurs exposés. https://www.anses.fr/fr/content/pollution-du-trafic-routier-des-risques-accrus-pour-les-travailleurs-exposes
- Novembre 2024. Des chercheurs du NIEHS (National Institute of Environmental Health Sciences) participent à une discussion mondiale sur la recherche concernant l'exposome humain. https://www.niehs.nih.gov/research/programs/geh/geh_newsletter/2024/11/articles/niehs-researchers-participate-in-global-discussion-on-human-exposome-research
- Décembre 2024. Un conférencier de Falk discute de nouvelles méthodes de détection des expositions environnementales. Andrea Baccarelli, Ph.D., a décrit comment l'épigénétique et les exosomes peuvent estimer les effets sur la santé de diverses expositions au cours de la vie. https://factor.niehs.nih.gov/2024/12/science-highlights/detecting-env-exposure

- 27 novembre IRSST : une fiche informative sur les risques pour la santé liés à l'industrie du recyclage électronique est désormais disponible. https://pharesst.irsst.qc.ca/fiches/121/
- Extrait newsletter PARC automne-hiver 2024. Promouvoir la sécurité des travailleurs : études professionnelles PARC dans le domaine de la gestion des déchets électroniques et des plastiques, et l'exposition aux médicaments cytotoxiques, aux produits de désinfection et de nettoyage et aux anesthésiques par inhalation sera évaluée dans le cadre de soins de santé hospitaliers dans 11 pays. https://www.eu-parc.eu/news/risk-assessment/advancing-worker-safety-parc-occupational-studies-waste-management-and?utm_source=hs_email&utm_medium=email&_hsenc=p2ANqtz-8xiw35IXVuqXcKeMP3VQA5tNhZUVMCH2rbj1v0QKBE6l3jdjNUebSXyPhKyvPbQWe2f1m5jBuXfkIhjcY7m7z4Kd3F4w
- 20 décembre 2024. Fédération of american scientists. Création d'un projet d'exposome national. https://fas.org/publication/creating-a-national-exposome-project/
- 27 janvier 2025. Lien vers le dossier de l'IRSST. L'IRSST publie une revue de littérature qui analyse la composition chimique des poussières de bois brûlé, une problématique dans le contexte des feux de forêt. Cette revue de littérature identifie des composés tels que le carbone, les oxydes, les métaux et, dans certains cas, de faibles concentrations d'hydrocarbures aromatiques polycycliques (HAP)

Sommaire

- **Reviews**

Barbey, C., Bonvallot, N., Clerc, F.
Health Outcomes Related to Multiple Exposures in Occupational Settings: A Review.
Safety and Health at Work 2024; Vol. 15 (4) p 382-395.

Individuals are constantly exposed to hazardous factors that can affect their health, the hazards encountered in the workplace can lead to the development of occupational diseases. Risk mitigation measures help to reduce the risks, but they are often designed without consideration of interactions between occupational exposures. Therefore, there is a need for research and it resulted in international research plans and programmes.
The aim of this scoping review is to provide an overview of the scientific results related to the link between multiple occupational exposures and human health outcomes. Sixtythree articles were reviewed. Research articles were included only if they mentioned: several combined exposures, the direct characterisation of each exposure, and exposure/health outcome associations. Seven activity sectors were identified: 'extraction and energy production and distribution', 'health care', 'banks, public administration and defence', 'chemical production', 'manufacturing industry', 'agriculture and food industry' and 'transport and logistics'. Six multiple exposures scenarios were identified: chemical (n = 35), chemical/physical-biomechanical (n = 22), chemical/psychosocial-organisational (n = 6), physical-biomechanical (n = 9), physical-biomechanical/psychosocial-organisational (n = 13), and psychosocial-organisational (n = 12). The health problems identified concern nervous, mental, respiratory, musculoskeletal, auditory and other systems. Eighty-eight of 97 (91%) multiple exposure/ health problem associations were reported to be statistically significant. Twenty studies (32%) provided specific risk prevention advice for multiple exposures. Prevention aimed at reducing risks to workers' health is still underdeveloped, further research is needed to improve prevention methods. No study was related to biological risk, and some other multiple exposures known to have health effects were not identified as well. This highlights the need for more multiple exposures research.

https://doi.org/10.1016/j.shaw.2024.10.004

****

Thaon, Isabelle
Agressions respiratoires des expositions aux contaminants professionnels et leurs conséquences sur la santé mentale.
Life Sciences [q-bio]. Université de Lorraine, 2024. HAL Id : tel-04843915, version 1.

De multiples activités professionnelles, en milieu agricole, industriel ou dans le secteur du bâtiment peuvent, ou ont pu, exposer les travailleurs à l'inhalation de gaz, poussières, fumées et/ou aérosols. Ces derniers peuvent de nature variable : particules minérales par exemple amiante ou silice, mélanges complexes de gaz et particules métalliques dans les fumées de soudage, particules végétales chez les agriculteurs ou les boulangers, bioaérosols constitués de micro-organismes bactériens ou fongiques chez les agriculteurs mais également chez les usineurs en cas de contaminations de fluides de coupe.
Ces expositions, facteurs d'agressions de l'appareil respiratoire peuvent favoriser l'apparition de pathologies diverses, variables selon la nature de l'exposition : troubles ventilatoires obstructifs (asthme, BPCO), pneumopathies interstitielles (pneumoconioses, pneumopathies d'hypersensibilité voire fibroses

pulmonaires idiopathiques) mais aussi, pour certaines expositions, de cancers. Ces derniers surviennent souvent plusieurs dizaines d'années après l'exposition pouvant engendrer un phénomène d'épée de Damoclès. Ainsi chez certains sujets ayant été exposés à l'amiante inclus dans des programmes de surveillance un impact sur la santé mentale (anxiété et dépression) et sur la santé perçue a être pu être observé. L'exploration des déterminants de cet impact sur la santé mentale et sur la santé perçue des expositions à l'amiante voire à d'autres cancérogènes professionnels mérite d'être approfondie.
https://hal.science/tel-04843915

****

Patel, P., Bello, D., Bello, A.
Identifying and Prioritizing Hazardous Chemicals in Construction Metal Structure Coating Systems: A Roadmap for Data-Driven Disease Prevention.
American Journal of Industrial Medicine 2024; Vol.

Introduction : Occupational exposure as a painter was classified by the International Agency for Research on Cancer (IARC) as a Group 1 carcinogen (carcinogenic to humans) in 1989. Chemical agents responsible for cancers and other illnesses among industrial painters are not well-documented.
The goal of this systematic review and synthesis was to document the chemistries of metal structure coating systems, summarize data gaps on occupational exposures and health effects among painters, and identify and prioritize hazardous chemicals to guide future exposure and occupational health studies, and ultimately disease prevention efforts.
Methods We reviewed coating products approved by the Northeast Protective Coating Committee (NEPCOAT) for use in steel bridges in New England, with a special focus on Part B of these reactive chemical systems, and related literature on exposures and health effects.
ResultsFrom the review of safety datasheets (SDS), we identified 61 unique CAS numbers belonging to different Part B chemical groups of isocyanate- and epoxy-based formulations, including amine hardeners, solvents, nanomaterials, and other additives. The list of identified ingredients contained 14 potent sensitizers, two IARC Group 1 known carcinogens, and 7 IARC Group 2B possible carcinogens. Cancers of the lungs, urinary bladder, liver, kidneys, and gastrointestinal system, allergic contact dermatitis, lung fibrosis, and asthma were some possible disease endpoints. Existing occupational exposure studies focused on solvent exposures, while exposure and biomonitoring studies of amine hardeners and other ingredients of concern in these formulations are lacking.
Conclusions : The list of chemicals of concern identified here, including sensitizers and carcinogens, can serve as a basis for analytical method development and field exposure assessment studies. A national multi-pronged strategy to reduce chemical exposures and health risks among construction painters is warranted, including research on exposure monitoring and reduction efforts, longitudinal epidemiological studies, and product reformulation.
https://doi.org/10.1002/ajim.23677

****

Alexander, B. M., Graydon, P. S., Pena, M., Feng, H. A., Beamer, B. R.
Hazardous exposures and engineering controls in the landscaping services industry.
Journal of Occupational and Environmental Hygiene Vol., p 1-14.

Landscapers are exposed to noise, carbon monoxide (CO), respirable dust, and respirable crystalline silica (RCS) generated from the tools they use. Although engineering controls are available to reduce these

exposures, no previous study has evaluated chronic exposures to landscapers in different work settings and compared exposures from landscaping tools with and without engineering controls.
This field study of workers in the landscaping services industry documented the occupational exposures of 80 participants at 11 varied worksites to noise, CO, respirable dust, and RCS using personal breathing zone sampling. Results were analyzed using SAS/STAT 14.1. Analysis of variance was used for normally distributed data; otherwise, nonparametric methods were used.
Most workers were overexposed to noise, with 94 of the 119 8-hr time-weighted average (TWA) noise exposures at or above the National Institute for Occupational Safety and Health (NIOSH) recommended exposure limit (REL) of 85 dBA. There were no statistically significant differences among different locations or occupations. No 8-hr TWA exposures to CO above the NIOSH REL were measured. Overexposures to RCS were measured at all locations where hardscaping (installing or maintaining non-living aspects of the landscape) was taking place.
This is the first known field study of this type to include hardscapers. The use of engineering controls such as dust capture or wet methods would reduce RCS exposures, but respiratory protection may still be needed. Task-based analysis of noise and CO exposure revealed that the loudest landscaping tools used in this study were hardscaping table saws, gas chainsaws, gas leaf blowers, chipper/shredders, gas string trimmers, and fuel mowers. Workers were exposed to significantly more noise and CO when using fuel-powered versions compared to battery-powered versions of leaf blowers, string trimmers, and chainsaws.
https://doi.org/10.1080/15459624.2024.2439810

****

- **Exposome – approche métabolomique**

Caballero-Casero, N., Ballesteros-Gomez, A. M., Rubio, S.
Supramolecular solvents: a gateway to all-in-one extractions in chemical exposomics.
Analytical and Bioanalytical Chemistry 2024; Vol. p

The characterization of the human chemical exposome through daily estimated intakes or biomonitoring has become paramount to understand the causal pathways leading to common diseases. The paradigm shift that has taken place in looking at health has moved research from the classical biomedical model based on "one exposure, one disease" to a more comprehensive approach based on multiple chemicals and low dose effects. For this purpose, untargeted and/or suspect analysis of chemicals based on liquid chromatography and high-resolution mass spectrometry (LC-HRMS) has been proposed as the most relevant strategy for sequencing the exposome. A key aspect in this respect is the development of unbiased sample preparation methods that efficiently concentrate the wide range of untargeted/suspected chemicals while minimizing interference from sample matrices.
Here, we aim to critically discuss the potential of tailored supramolecular solvents (SUPRAS) for achieving all-in-one extractions in chemical exposomics, as an alternative to overcome the limitations of the current sample treatment strategies, on the basis of their intrinsic properties and the applications reported so far.
https://doi.org/10.1007/s00216-024-05645-7

****

Healy, D. R., Zarei, I., Mikkonen, S., Soininen, S., Viitasalo, A., Haapala, E. A.*, et al.*
Longitudinal associations of an exposome score with serum metabolites from childhood to adolescence.
Communications Biology 2024; Vol. 7 (1) p 890.

Environmental and lifestyle factors, including air pollution, impaired diet, and low physical activity, have been associated with cardiometabolic risk factors in childhood and adolescence. However, environmental and lifestyle exposures do not exert their physiological effects in isolation.
This study investigated associations between an exposome score to measure the impact of multiple exposures, including diet, physical activity, sleep duration, air pollution, and socioeconomic status, and serum metabolites measured using LC-MS and NMR, compared to the individual components of the score. A general population of 504 children aged 6–9 years at baseline was followed up for eight years. Data were analysed with linear mixed-effects models using the R software. The exposome score was associated with 31 metabolites, of which 12 metabolites were not associated with any individual exposure category.
These findings highlight the value of a composite score to predict metabolic changes associated with multiple environmental and lifestyle exposures since childhood.
https://doi.org/10.1038/s42003-024-06146-0

****

Edlund, J., Sdougkou, K., Papazian, S., Wu, W. Y.-Y., Martin, J. W., Harlid, S.
Chemical exposomics in biobanked plasma samples and associations with breast cancer risk factors.
Journal of Exposure Science & Environmental Epidemiology 2024; Vol.p

The chemical exposome includes exposure to numerous environmental and endogenous molecules, many of which have been linked to reproductive outcomes due to their endocrine-disrupting properties. As several breast cancer risk factors, including age and parity, are related to reproduction, it is imperative to investigate the interplay between such factors and the chemical exposome prior to conducting large scale exposome-based breast cancer studies.
This pilot study aimed to provide an overview of the chemical exposome in plasma samples from healthy women and identify associations between environmental exposures and three risk factors for breast cancer: age, parity, and age at menarche.
Plasma samples (n = 161), were selected based on reproductive history from 100 women participating in the Northern Sweden Health and Disease Study, between 1987 and 2006. Samples were analyzed by liquid chromatography high-resolution mass spectrometry (LC-HRMS) for 77 priority target analytes including contaminants and hormones, with simultaneous untargeted profiling of the chemical exposome and metabolome. Linear mixed effects models were applied to test associations between risk factors and chemical levels.
Fifty-five target analytes were detected in at least one individual and over 94,000 untargeted features were detected across all samples. Among untargeted features, 430 could be annotated and were broadly classified as environmental (246), endogenous (167) or ambiguous (17). Applying mixed effect models to features detected in at least 70% of the samples (16,778), we found seven targeted analytes (including caffeine and various per- and poly-fluoroalkyl substances) and 38 untargeted features, positively associated with age. The directionality of these associations reversed for parity, decreasing with increasing births. Seven separate targeted analytes were associated with age at menarche.
This study demonstrates how a comprehensive chemical exposome approach can be used to inform future research prioritization regarding associations between known and unknown substances, reproduction, and breast cancer risk.
https://doi.org/10.1038/s41370-024-00736-0

****

Pang, Z., Viau, C., Fobil, J. N., Basu, N., Xia, J.
Comprehensive Blood Metabolome and Exposome Analysis, Annotation, and Interpretation in E-Waste Workers. In: Metabolites. 2024. Vol. 14 Issue 12

Background: Electronic and electrical waste (e-waste) production has emerged to be of global environmental public health concern. E-waste workers, who are frequently exposed to hazardous chemicals through occupational activities, face considerable health risks.
Methods: To investigate the metabolic and exposomic changes in these workers, we analyzed whole blood samples from 100 male e-waste workers and 49 controls from the GEOHealth II project (2017–2018 in Accra, Ghana) using LC-MS/MS. A specialized computational workflow was established for exposomics data analysis, incorporating two curated reference libraries for metabolome and exposome profiling. Two feature detection algorithms, asari and centWave, were applied.
Results: In comparison to centWave, asari showed better sensitivity in detecting MS features, particularly at trace levels. Principal component analysis demonstrated distinct metabolic profiles between e-waste workers and controls, revealing significant disruptions in key metabolic pathways, including steroid hormone biosynthesis, drug metabolism, bile acid biosynthesis, vitamin metabolism, and prostaglandin biosynthesis. Correlation analyses linked metal exposures to alterations in hundreds to thousands of metabolic features. Functional enrichment analysis highlighted significant perturbations in pathways related to liver function, vitamin metabolism, linoleate metabolism, and dynorphin signaling, with the latter being observed for the first time in e-waste workers.
Conclusions: This study provides new insights into the biological impact of prolonged metal exposure in e-waste workers.
https://doi.org/10.3390/metabo14120671

****

Drahi E., Le Noc Y, Bergua G., Dumoulin M, Steyer E., Scali C.
L'exposome, une vision globale de la santé des populations. Quelles implications dans la pratique ?
Médecine 2024; Vol. 20 (9) p 403-406.

Le concept d'exposome se définit comme englobant la totalité des expositions subies par un individu tout au long de sa vie, dès sa conception, expositions non seulement chimiques (pollution), mais aussi environnementales (climat, pollution sonore), voire sociétales (travail, transports, vie en société) ou comportementales… Toutes les catégories sociales ne sont pas égales face aux problèmes de santé. Ce concept récent a ainsi de nombreuses implications dans les domaines de la recherche, de l'épidémiologie, des politiques de santé publique, pour définir de vraies politiques d'évaluation des risques et de prévention. Comment concrètement intégrer ce concept dans la pratique de soins ?
DOI : 10.1684/med.2024.1035

****

Shahbazi, Z., Nowaczyk, S.
Towards personalized cardiometabolic risk prediction: A fusion of exposome and AI.
Heliyon 2025; Vol. 11 (1), p e40859.

The influence of the exposome on major health conditions like cardiovascular disease (CVD) is widely recognized. However, integrating diverse exposome factors into predictive models for personalized health

assessments remains a challenge due to the complexity and variability of environmental exposures and lifestyle factors. A machine learning (ML) model designed for predicting CVD risk is introduced in this study, relying on easily accessible exposome factors.
This approach is particularly novel as it prioritizes non-clinical, modifiable exposures, making it applicable for broad public health screening and personalized risk assessments. Assessments were conducted using both internal and external validation groups from a multi-center cohort, comprising 3,237 individuals diagnosed with CVD in South Korea within twelve years of their baseline visit, along with an equal number of participants without these conditions as a control group. Examination of 109 exposome variables from participants' baseline visits spanned physical measures, environmental factors, lifestyle choices, mental health events, and early-life factors. For risk prediction, the Random Forest classifier was employed, with performance compared to an integrative ML model using clinical and physical variables. Furthermore, data preprocessing involved normalization and handling of missing values to enhance model accuracy. The model's decision-making process were using an advanced explainability method.
Results indicated comparable performance between the exposome-based ML model and the integrative model, achieving AUC of 0.82(+/-)0.01, 0.70(+/-)0.01, and 0.73(+/-)0.01. The study underscores the potential of leveraging exposome data for early intervention strategies. Additionally, exposome factors significant in identifying CVD risk were pinpointed, including daytime naps, completed full-time education, past tobacco smoking, frequency of tiredness/unenthusiasm, and current work status.
DOI: 10.1016/j.heliyon.2024.e40859

****

Moeller Kynde, T., Wan, W., Garcia, J., Alcaraz, V., Urrutia, I., Martinez-Moratalla, J.*, et al.*
Working-life exposome and new-onset COPD: An exposome-wide association study (ExWAS).
European Respiratory Journal Vol. 64 (suppl 68), p OA974.

Introduction: COPD is a leading cause of death worldwide and linked to occupational exposures. We aimed to explore the link between working-life exposome and new-onset COPD, starting with an exposome-wide association study (ExWAS).
Method: We included two European multi-centre population-based cohorts, ECRHS and Constances. ECRHS began in 1992 (participants 20-44 years) with two follow-ups at ~10 and ~20 years. Constances, baseline 2012-2020 (18-69 years), one follow-up at ~4 years. COPD was defined by FEV1/FVC<Lower limit of normal and at least one respiratory symptom, excluding those with COPD at baseline. Cumulative exposure was assessed at each follow-up for 49 occupational exposures using 5 job exposure matrices. The ExWAS was conducted with discrete-time hazard models adjusted for sex, weight, pack-years of smoking, parental asthma, years between follow-up, physical activity and center.
Results: Information was available for n=4065, male 51% (ECRHS) and n=5855, male 49% (Constances). In ECRHS we found increased risk of new-onset COPD (adjusted Odds ratios; 95% CI) for exposure to: exhaust fumes (1.12; 1.03-1.21), asbestos (1.13; 1.02-1.24), gas fumes (1.13; 1.1-1.25), biological dust (1.11; 1.0-1.22), heavy lifting (1.13; 1.0-1.25), mineral dust (1.11; 1.0-1.23), and house dust mites (1.07; 1.0-1-15). There was no evidence for effect-modification by asthma status. No clear associations were found for Constances.
Conclusion: Occupational exposures was linked to increased risk of COPD in ECRHS only, probably due to an older population and longer time of follow-up compared to Constances. This ExWAS set the stage for the next analytical step, assessing the joint effect of the working life-exposme.
https://doi.org/10.1183/13993003.congress-2024.OA974

****

Tartaglia, M., Costet, N., Audignon-Durand, S., Carles, C., Descatha, A., Falkstedt, D.*, et al.*
Profiles of the maternal occupational exposome during pregnancy and associations with intrauterine growth: Analysis of the French Longitudinal Study of Children - ELFE study.
Environmental research 2024; Vol. 267, p 120669.

BACKGROUND: Numerous agents in the workplace are suspected of impairing fetal growth. To date, no epidemiological studies have specifically described the occupational exposome during pregnancy.; OBJECTIVE: The objectives were to determine maternal occupational exposome profiles and study their associations with intrauterine growth characteristics measured by small for gestational age (SGA), birthweight (BW), and head circumference (HC).
METHODS: We used data from the French national ELFE cohort. Occupational exposures to 47 agents (chemical, physical, biological, biomechanical, organizational and psychosocial), were identified using job exposure matrices. Mothers were classified as occupationally not exposed, uncertainly exposed, or exposed depending on their probability of exposure. Outcomes of interest were BW, SGA and HC. Maternal profiles of the occupational exposome were determined using hierarchical clustering of principal components. Associations between profiles and intrauterine growth outcomes were studied using linear or logistic regression models adjusted for potential confounders. Analyses were carried out depending on whether mothers stopped working during pregnancy.;
RESULTS: The 12,851 included women were exposed to a median of 6 factors. Four occupational exposome profiles were identified, characterized by "low exposure, stress at work"; "strenuous, high organization, low decision"; "postural constraints, psychosocial factors", "postural and strength constraints, chemical and biological factors". In multivariate analyses, and among women who stopped working during the third trimester of pregnancy, analyses found associations between the profile "postural constraints, psychosocial factor" and SGA, and HC. None of the other exposure profiles were statistically significantly associated with foetal growth outcomes.;
CONCLUSION: The results show that the specific profile "postural constraints, psychosocial factors" may increase the risk of foetal growth retardation. Although these results need to be replicated, this study provides a first better understanding of the exposome of pregnant women at the workplace which may help to better adapt prevention strategies.
https://doi.org/10.1016/j.envres.2024.120669

****

Pang, Z. Q., Xu, L., Viau, C., Lu, Y., Salavati, R., Basu, N., Xia, J. G.
MetaboAnalystR 4.0: a unified LC-MS workflow for global metabolomics.
Nature Communications 2024; Vol. 15 (1) p

The wide applications of liquid chromatography - mass spectrometry (LC-MS) in untargeted metabolomics demand an easy-to-use, comprehensive computational workflow to support efficient and reproducible data analysis. However, current tools were primarily developed to perform specific tasks in LC-MS based metabolomics data analysis.
Here we introduce MetaboAnalystR 4.0 as a streamlined pipeline covering raw spectra processing, compound identification, statistical analysis, and functional interpretation. The key features of MetaboAnalystR 4.0 includes an auto-optimized feature detection and quantification algorithm for LC-MS1 spectra processing, efficient MS2 spectra deconvolution and compound identification for data-dependent or data-independent acquisition, and more accurate functional interpretation through integrated spectral annotation. Comprehensive validation studies using LC-MS1 and MS2 spectra obtained from standards

mixtures, dilution series and clinical metabolomics samples have shown its excellent performance across a wide range of common tasks such as peak picking, spectral deconvolution, and compound identification with good computing efficiency.
Together with its existing statistical analysis utilities, MetaboAnalystR 4.0 represents a significant step toward a unified, end-to-end workflow for LC-MS based global metabolomics in the open-source R environment. Several bottlenecks exist in metabolomics data analysis. Here, the authors present MetaboAnalystR 4.0 as a unified workflow for LC-MS untargeted metabolomics. It highlights significant improvements in LC-MS2 spectral processing and functional analysis, providing an end-to-end computational pipeline.
https://doi.org/10.1038/s41467-024-48009-6

****

Wu, T., Zhao, L., Ren, M., He, S., Zhang, L., Fang, M., Wang, B.
Small-Sample Learning for Next-Generation Human Health Risk Assessment: Harnessing AI, Exposome Data, and Systems Biology.
Environmental Science & Technology 2025; Vol. 59 (1), p 5-10.

La réalisation d'évaluations des risques pour la santé humaine (ERS) liées à l'exposition environnementale présente des défis importants, en particulier lors de l'application de méthodes épidémiologiques traditionnelles aux mégadonnées d'exposomes. Ces données englobent un large éventail de facteurs environnementaux exogènes (par exemple, les polluants organiques persistants, les perturbateurs endocriniens, les métaux, les polluants de l'air ambiant, les bactéries et le bruit) et d'informations biologiques endogènes (par exemple, l'épigénome, le transcriptome, le protéome, le métabolome, le microbiote intestinal, l'inflammation et le stress oxydatif). (1) Par exemple, la base de données sur les exposomes humains (HExpMetDB) a compilé > 20 000 produits chimiques et classé par ordre de priorité 13 441 produits chimiques sur la base du quotient de danger probabiliste et 7770 produits chimiques sur la base de l'indice de risque. (2) Notre base de données d'exposomes récemment développée comprenait ∼119 millions d'expositions et 17 186 sous-types de maladies provenant de sources bien établies (voir la base de données ExposomeX à http://www.exposomex.cn/#/database101). De plus, nous avons proposé TOXRIC (https://toxric.bioinforai.tech/), une base de données contenant des données toxicologiques complètes, des données d'attributs standardisées, des repères pratiques, une visualisation informative des représentations moléculaires et une interface de fonction intuitive. (3) La base de données TOXRIC contient 113 372 produits chimiques répartis dans 13 catégories de toxicité, 1474 paramètres de toxicité couvrant les paramètres in vivo et in vitro, et 39 types de caractéristiques. Pour obtenir la relation de cause à effet, ces méthodes nécessitent souvent beaucoup de temps et de ressources en raison de l'exigence d'un échantillon de grande taille, de suivis à long terme, d'une collecte de données approfondie et d'une analyse expérimentale coûteuse.

https://doi.org/10.1021/acs.est.4c11832

****

Isola, S., Murdaca, G., Brunetto, S., Zumbo, E., Tonacci, A., Gangemi, S.
The Use of Artificial Intelligence to Analyze the Exposome in the Development of Chronic Diseases: A Review of the Current Literature.
Informatics-Basel 2024; Vol. 11 (4) p

The "Exposome" is a concept that indicates the set of exposures to which a human is subjected during their

lifetime. These factors influence the health state of individuals and can drive the development of Noncommunicable Diseases (NCDs). Artificial Intelligence (AI) allows one to analyze large amounts of data in a short time. As such, several authors have used AI to study the relationship between exposome and chronic diseases. Under such premises, this study reviews the use of AI in analyzing the exposome to understand its role in the development of chronic diseases, focusing on how AI can identify patterns in exposure-related data and support prevention strategies.
To achieve this, we carried out a search on multiple databases, including PubMed, ScienceDirect, and SCOPUS, from 1 January 2019 to 31 May 2023, using the MeSH terms (exposome) and ('Artificial Intelligence' OR 'Machine Learning' OR 'Deep Learning') to identify relevant studies on this topic. After completing the identification, screening, and eligibility assessment, a total of 18 studies were included in this literature review. According to the search, most authors used supervised or unsupervised machine learning models to study multiple exposure factors' role in the risk of developing cardiovascular, metabolic, and chronic respiratory diseases. In some more recent studies, authors also used deep learning.
Furthermore, the exposome analysis is useful to study the risk of developing neuropsychiatric disorders or evaluating pregnancy outcomes and child growth. Understanding the role of the exposome is pivotal to overcome the classic concept of a single exposure/disease. The application of AI allows one to analyze multiple environmental risks and their combined effects on health conditions. In the future, AI could be helpful in the prevention of chronic diseases, providing new diagnostic, therapeutic, and follow-up strategies.
https://doi.org/10.3390/informatics11040086

****

Gu, Y., Zheng, S., Huang, C., Cao, X., Liu, P., Zhuang, Y.*, et al.*
Microbial colony sequencing combined with metabolomics revealed the effects of chronic hexavalent chromium and nickel combined exposure on intestinal inflammation in mice.
The Science of the total environment 2024; Vol. 915, p 169853

The pollution and toxic effects of hexavalent chromium [Cr(VI)] and divalent nickel [Ni(II)] have become worldwide public health issues. However, the potential detailed effects of chronic combined Cr(VI) and Ni exposure on colonic inflammation in mice have not been reported. In this study, 16S rDNA sequencing, metabolomics data analysis, qPCR and other related experimental techniques were used to comprehensively explore the mechanism of toxic damage and the inflammatory response of the colon in mice under the co-toxicity of chronic hexavalent chromium and nickel.
The results showed that long-term exposure to Cr(VI) and/or Ni resulted in an imbalance of trace elements in the colon of mice with significant inflammatory infiltration of tissues. Moreover, Cr(VI) and/or Ni poisoning upregulated the expression levels of IL-6, IL-18, IL-1β, TNF-α, IFN-γ, JAK2 and STAT3 mRNA, and downregulated IL-10 mRNA, which was highly consistent with the trend in protein expression. Combined with multiomics analysis, Cr(VI) and/or Ni could change the α diversity and β diversity of the gut microbiota and induce significant differential changes in metabolites such as Pyroglu-Glu-Lys, Val-Asp-Arg, stearidonic acid, and 20-hydroxyarachidonic acid. They are also associated with disorders of important metabolic pathways such as lipid metabolism and amino acid metabolism. Correlation analysis revealed that there was a significant correlation between gut microbes and metabolites ($P < 0.05$).
In summary, based on the advantages of comprehensive analysis of high-throughput sequencing sets, these results suggest that chronic exposure to Cr(VI) and Ni in combination can cause microbial flora imbalances, induce metabolic disorders, and subsequently cause colonic damage in mice. These data provide new insights into the toxicology and molecular mechanisms of Cr(VI) and Ni.
https://doi.org/10.1016/j.scitotenv.2023.169853

****

Haque, E., Adamcakova-Dodd, A., Jing, X. F., Wang, H., Jarmusch, A. K., Thorne, P. S.
Multi-omics inhalation toxicity assessment of urban soil dusts contaminated by multiple legacy sources of lead (Pb).
Journal of Hazardous Materials 2024 5 December, Vol. 480 : 136120

Although animal studies have evaluated lead (Pb) toxicity, they are limited to soluble forms, such as Pb-acetate, which do not reflect the range found in the exposome. Recent studies on Pb speciation of residential soils in urban areas revealed that the initial Pb sources are not persistent and are extensively repartitioned into adsorbed forms of Pb rather than insoluble phosphates. We investigated the inhalation and neurological toxicity of dusts generated from a surficial soil sample collected from a residential site with an exposomic mixture of various Pb species, both adsorbed phases (Fe and Mn oxide, humate bound Pb) and mineral phases (Pb hydroxycarbonate, pyromorphite, galena). Mice inhaled East Chicago dust (ECD) generated from a composite soil sample for 4 h/ day, 7 days/week, for 4 weeks. Mice were necropsied immediately, 1, 14 and 30 days post exposure to evaluate both toxicity and recovery. Exposure to ECD caused changes in memory and spatial learning in the Morris Water Maze test. RNAseq analysis of the hippocampus region revealed multiple differentially expressed genes and impacts on pathways involved in ion channel complexes, and neuron-to-neuron synapse. Metabolomics analysis of plasma highlighted significant alterations in metabolic processes immediately after exposure that resolved after 14 days of rest.
https://doi.org/10.1016/j.jhazmat.2024.136120

****

- ## Biomarqueurs des polyexpositions

Jo, E. K., Kwon, J., Kang, D. H., Jeon, J., Kho, Y., Shin, M. Y., Kim, S.
Suspect screening candidate exposure biomarkers of acetyl tributyl citrate and acetyl triethyl citrate after human oral administration.
Environment International 2024; Vol. 193,p

Acetyl tributyl citrate (ATBC) and acetyl triethyl citrate (ATEC) are widely used as plasticizers, but their metabolites as exposure biomarkers for biomonitoring, as well as approximate human metabolic pathways, are not well understood. This study addresses this knowledge gap by conducting suspect screening to propose specific metabolites in human urine as potential biomarkers of exposure and explore their kinetic profiles.
Ten volunteers were administered deuterium labeled ATBC (ATBC-d3) and seven received ATEC or deuterium labeled ATEC (ATEC-d3), with urine samples collected over 48 h post-administration. Employing ultra-performance liquid chromatography coupled to quadrupole-time-of-flight mass spectrometry (UPLC-qTOF/MS), six metabolites of ATBC were consistently detected, including (OH)3-ATBC-d3, ADBC-d3, OH-ADBC-d3, DBC, OH-DBC, and OHDBA. For ATEC, four metabolites were identified: ADEC-d3, AMEC-d3, OH-ADEC-d3, and DEC. Based on their high detection frequency, relative response, and specificity to their parent compounds, ADBC-d3 and OH-ADBCd3 were identified as promising candidate biomarkers for ATBC exposure, while ADEC-d3 emerged as a suitable biomarker for ATEC. Estimated urinary elimination half-lives ranged from 1.0 to 9.9 h for ATBC metabolites and 1.6 to 3.0 h for ATEC metabolites. One-compartment kinetic modeling provided preliminary insights into metabolite kinetics.
This research advances the understanding of ATBC and ATEC metabolism in humans, providing a foundation for future exposure assessments and toxicological studies. The identified biomarkers and preliminary metabolic profiles offer valuable starting points for biomonitoring and risk assessment of these alternative

plasticizers.
https://doi.org/10.1016/j.envint.2024.109062

****

Li, S. Q., Liao, X. J., Ma, R., Deng, N., Wu, H. M., Zhang, Z. R., *et al.*
Effects of Co-Exposure to Benzene, Toluene, and Xylene, Polymorphisms of microRNA Genes, and Their Interactions on Genetic Damage in Chinese Petrochemical Workers.
Toxics 2024; Vol. 12 (11),p

Benzene, toluene, and xylene (BTX) co-exist in human environments, yet their individual and combined effects on genetic damage at low exposure levels are not fully understood. Additionally, single nucleotide polymorphisms in microRNAs (mirSNPs) might be involved in cancer etiology by affecting the related early health damage. To investigate the influence of BTX exposure, mirSNPs, and their interactions on genetic damage, we conducted a cross-sectional study in 1083 Chinese petrochemical workers, quantifying the BTX cumulative exposure levels and multiple genetic damage biomarkers. Additionally, we genotyped multiple common mirSNPs.
Benzene and a BTX mixture were positive associated with the olive tail moment (OTM) and tail DNA% ($p < 0.05$). Higher levels of toluene and xylene enhanced the association of benzene with genetic damage levels. Genotypes and/or mutant allele counts of miR-4482-related rs11191980, miR-4433-related rs136547, miR-27a-related rs2594716, miR-3130-related rs725980, and miR-3928-related rs878718 might significantly influence genetic damage levels. Stronger effect estimates of benzene/BTX exposure were found in carriers of miR-196a-2-related rs11614913 heterozygotes and of wild homozygotes of miR-1269b-related rs12451747, miR-612-related rs12803915, and miR-4804-related rs266437.
Our findings provide further support of the involvement of BTX co-exposure, mirSNPs, and their gene-environment interactions in determining the severity of DNA strand break in a complex manner.
https://doi.org/10.3390/toxics12110821

****

Moro, A. M., Brucker, N., Goethel, G., Flesch, I., Nascimento, S., Charão, M., *et al.*
The Influence of Blood Titanium Levels on DNA Damage in Brazilian Workers Occupationally Exposed to Different Chemical Agents.
Biological Trace Element Research 2024; Vol., p

Occupational exposure to pollutants may cause health-damaging effects in humans. Genotoxicity assays can be used to detect the toxic effects of pollutants. In the present study, we evaluated genetic damage in three populations occupationally exposed to benzene, pyrenes, and agrochemicals and assessed the possible influence of titanium (Ti) co-exposure.
A total of 275 subjects were enrolled in this study. The occupationally exposed population was composed of 201 male individuals, divided into three different groups: gas station attendants (GSA group) (n = 76), taxi drivers (TD group) (n = 97), farmers (farmers group) (n = 28), and control (n = 74). Biomarkers of exposure and effect were investigated such as AChe, BuChE, t,t-muconic acid (t,t-MA), and 1-hydroxypyrene (1-OHP). Ti levels in blood were higher in all the workers compared with the control group. DNA damage evaluated by comet assay was higher in the taxi drivers and farmers than in the controls, and the frequency of micronucleate buccal cells was higher in the gas station attendants and taxi drivers than in the controls. Correlations were found among occupational exposure time and biomarkers of exposure, genotoxicity biomarkers, and blood Ti levels. Our results demonstrated Ti co-exposure in the gas station attendants, taxi drivers, and farmers, and blood Ti levels were linked with the respective biomarkers of exposure.

Additionally, tools through machine learning corroborated these findings, and Ti was the factor that contributed to DNA damage.
Thus, the present study indicates the role of Ti in occupational settings and interactions with already known major xenobiotics present in the occupational environment contributing to genotoxicity.
https://doi.org/10.1007/s12011-024-04472-2

****

Kasper-Sonnenberg, M., Palmke, C., Wrobel, S., Bruning, T., Murawski, A., Apel, P.*, et al.*
Plasticizer exposure in Germany from 1988 to 2022: Human biomonitoring data of 20 plasticizers from the German Environmental Specimen Bank.
Environment international 2024; Vol. 195, p 109190.

The German Environmental Specimen Bank (ESB) annually archives 24-h urine samples since the early 1980s. In this study, we analyzed 420 of these samples from the years 2014 to 2022 for metabolites of 18 phthalates and two substitutes. We merged the new data with the data from previous measurement campaigns to a combined dataset of 1825 samples covering a 35-year period from 1988 to 2022 to investigate time trends, calculate daily intakes and perform an anti-androgenic mixture risk assessment.
With the extended set of 41 biomarkers, we are now able to monitor the exposure to all EU-labelled reprotoxic phthalates. Most phthalate exposures continued to decrease since first measurements in the 80s, with biggest drops for DnBP (96.6%) and DEHP (90.9%). DiNP and DiDP, seen on the rise in earlier campaigns, now declined. Exposures to the newly included, reprotoxic phthalates were generally negligible. Regarding mixture risk, 5% of the highly exposed still exceeded the Hazard Index (HI) of 1 in 2009. In the current measurement campaign only three individuals (0.7%) exceeded the HI of 1 (with exceedances still driven by DEHP and DnBP). In 2022, 20% of the individuals still had an HI > 0.2, which we propose as a benchmark for interpreting phthalate mixture risk, considering concurrent exposures to other anti-androgens. Exposure to the substitutes DINCH and DEHTP continues to increase, with daily intakes of DEHTP exceeding those of DEHP since 2018. Compared with the United States (US) National Health and Nutrition Examination Survey (NHANES) phthalate exposures seem to align, except for DEHTP with up to ten times higher levels in the US.
Human biomonitoring (HBM) is the ideal tool to capture actual mixture exposures per individual, integrating all external exposure sources and pathways, thus we will continue to use HBM in exposure and risk assessment of phthalates and other (anti-androgenic) chemicals.

https://doi.org/10.1016/j.envint.2024.109190

****

Lu, P., He, R., Wu, Y., Wu, B., Li, H., He, C.*, et al.*
Urinary metabolic alterations associated with occupational exposure to metals and polycyclic aromatic hydrocarbons based on non-target metabolomics.
Journal of hazardous materials 2025; Vol. 487 p 137158.

Long-term occupational exposure to metals and organics have been reported to be under great health risks. However, limited data are available on the molecular mechanism between combined exposure to metals and polycyclic aromatic hydrocarbons (PAHs) and harmful health effects. In present work, non-target metabolomics study was conducted based on urine samples from nonferrous metal smelting workers (n = 207), surrounding residents (n = 180), and the control residents (n = 187) by using ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UHPLC-

QTOF-MS). Differential and correlation analyses among metabolic features indicate that total 22 differential metabolites in smelting workers were associated ($p < 0.05$) with metal and PAH exposure. Particularly, amino acid metabolism was strongly disturbed, and other metabolic pathways, including steroid hormone biosynthesis, citrate cycle, and pantothenate and coenzyme A (CoA) biosynthesis were also perturbed. Among them, steroid hormone biosynthesis was more affected by PAH exposure than metals, especially for hydroxyphenanthrene. These altered pathways were closely associated with oxidative stress, inflammation, and energy metabolism disorder.
Additionally, our results indicate that endogenous metabolism in surrounding residents were also affected by nonferrous metal smelting activities to some extent. Our work provides valuable insights into molecular mechanisms of adverse health effects probably induced by combined exposure to metals and PAHs.

https://doi.org/10.1016/j.jhazmat.2025.137158

****

- ## Modèles, méthodologies, outils de biomonitoring

Lai, Y. J., Ay, M., Miller, G. W., Sarkar, S., Carolina Duarte, H.
Seminar: Functional Exposomics and Mechanisms of Toxicity-Insights - Insights from Model Systems and NAMs.
Environmental Health Perspectives 2024; Vol. 132 (9) p

BACKGROUND : Significant progress has been made over the past decade in measuring the chemical components of the exposome, providing transformative population-scale frameworks in probing the etiologic link between environmental factors and disease phenotypes. While the analytical technologies continue to evolve with reams of data being generated, there is an opportunity to complement exposome-wide association studies (ExWAS) with functional analyses to advance etiologic search at organismal, cellular, and molecular levels.
OBJECTIVES : Exposomics is a transdisciplinary field aimed at enabling discovery-based analysis of the nongenetic factors that contribute to disease, including numerous environmental chemical stressors. While advances in exposure assessment are enhancing population-based discovery of exposome-wide effects and chemical exposure agents, functional screening and elucidation of biological effects of exposures represent the next logical step toward precision environmental health and medicine. In this work, we focus on the use, strategies, and prospects of alternative approaches and model systems to enhance the current human exposomics framework in biomarker search and causal understanding, spanning from bench-based non-mammalian organisms and cell culture to computational new approach methods (NAMs).
DISCUSSION : We visit the definition of the functional exposome and exposomics and discuss a need to leverage alternative models as opposed to mammalian animals for delineating exposome-wide health effects. Under the "three Rs" principle of reduction, replacement, and refinement, model systems such as roundworms, fruit flies, zebrafish, and induced pluripotent stem cells (iPSCs) are advantageous over mammals (e.g., rodents or higher vertebrates). These models are cost-effective, and cell-specific genetic manipulations in these models are easier and faster, compared to mammalian models. Meanwhile, in silico NAMs enhance hazard identification and risk assessment in humans by bridging the translational gaps between toxicology data and etiologic inference, as represented by in vitro to in vivo extrapolation (IVIVE) and integrated approaches to testing and assessment (IATA) under the adverse outcome pathway (AOP) framework.
https://doi.org/10.1289/ehp13120

****

Gastellu, T., Le Bizec, B., Rivière, G.
Integrating the lifelong exposure dimension of a chemical mixture into the risk assessment process. Application to trace elements.
Food and Chemical Toxicology 2025; Vol. 195 p 115111.

Lifelong, the general population is exposed to mixtures of chemicals. Most often, risk assessment is performed to estimate the probability of adverse effects in the population using external exposures to a single chemical and considering one route of exposure. To estimate whole exposure to a chemical, human biomonitoring studies are used to measure chemical concentrations in biological matrices. The limitations of these studies are that it is not possible to distinguish the sources or the routes of exposure. Moreover, only the concentrations of a limited number of chemicals are usually determined due to the associated cost.
In this study, a methodology has been developed to estimate the internal exposures of the population to a mixture of trace elements (inorganic As, Cd, Pb and Hg) throughout lifetime. This methodology uses realistic lifetime exposure trajectories coupled to physiological based kinetic modeling, considering several sources of exposure. Then, the estimated biomarkers of exposure were compared to human biomonitoring data to estimate the robustness of the methodology. Finally, risk characterization was performed based on the simulated biomarkers of exposure considering an additive effect of chemicals. This methodology allows to determine the contribution of chemicals to the overall risk of renal effect.
https://doi.org/10.1016/j.fct.2024.115111

****

Ghozal, M., Delvert, R., Adel-Patient, K., Tafflet, M., Annesi-Maesano, I., Crépet, A.*, et al.*
Dietary exposure to mixtures of chemicals in the first year of life and allergic and respiratory diseases up to 8 years in the French EDEN mother-child cohort.
Food and Chemical Toxicology 2025; Vol. 196, p 115167.

Exposure to environmental chemicals has been associated with higher risk of childhood allergies. This study aimed to examine the association between infant's dietary exposure to mixtures of chemicals and allergic and respiratory multimorbidity in childhood. Dietary exposures were assessed at 8 and 12 months in 724 and 745 children of the EDEN cohort. Allergic and respiratory multimorbidity clusters were identified using latent class analyses. Associations between dietary exposure to mixtures of chemicals and allergic clusters were assessed by adjusted multinomial logistic regressions.
At 8 months, higher exposure to a mixture of furans, trace elements, dioxins and PAHs was positively associated with the “asthma only” cluster, while moderate exposure to a mixture of PAHs, pesticides, PCBs and acrylamide was negatively associated with this cluster. A mixture of PCBs and BFRs was positively associated with the “multi-morbidity” cluster. Exposure to a mixture of pesticides and trace elements was positively associated with the “allergy without asthma” cluster. At 12-months, higher exposure to a mixture of trace elements and pesticides was positively associated with “multi-morbidity” cluster.
The differences in findings between the two ages suggest the need for further studies to explore this critical window of chemical exposure and its impact on children's health.
https://doi.org/10.1016/j.fct.2024.115167

****

Iglesias-Gonzalez, A., Appenzeller, B. M. R.
Comprehensive analysis, comprehensive understanding: The benefit of widening the scope to uncover the complexity of human chemical exposome and tailor personalized risk assessment.
Science of The Total Environment 2025; Vol. 958, p 178111.

While biomonitoring approaches are frequently employed for assessing chemical exposure, many of them are constrained to a limited number of target chemicals, running counter to our current understanding of interactions within chemical mixtures and the growing evidence of multiple exposures within human populations. Although authors agree on the need for more comprehensive methodologies, literature provides insufficient evidence of the multifaceted nature of exposure and of the benefit of widening the analytical scope to improve exposure assessment. Moreover, although multiple exposures are generally admitted, very few are known on the scale of the human chemical exposome.
Here, we illustrate how increasing the number of chemicals possibly captured improves the information on exposure. Through a literature review centered on studies utilizing hair analysis to assess exposure to anthropogenic organic pollutants, we provide here the first demonstration of how expanding the number of compounds analyzed in biomonitoring methods enhances our understanding of the chemical exposome. The results not only underscore the prevalence of multiple exposures but also reveal distinct exposure patterns within various demographic groups. Utilizing extrapolated biomonitoring data, we introduce a novel approach to estimate the number of chemicals to which humans can be simultaneously exposed. This biomonitoring-based approach is the first one relying on data derived from human samples rather than indirect metrics such as sales figures or registered chemicals. Eventually, we draw upon results from studies conducted in our team to illustrate local specificities in exposure among different populations, emphasizing the complexity of risk assessment while implemented in prevention strategies.
https://doi.org/10.1016/j.scitotenv.2024.178111

****

Jairi, I., Rekbi, A., Ben-Othman, S., Hammadi, S., Canivet, L., Zgaya-Biau, H.
Enhancing particulate matter risk assessment with novel machine learning-driven toxicity threshold prediction.
Engineering Applications of Artificial Intelligence 2025; Vol. 139, p

Airborne particulate matter (PM) poses significant health risks, necessitating accurate toxicity threshold determination for effective risk assessment. This study introduces a novel machine-learning (ML) approach to predict PM toxicity thresholds and identify the key physico-chemical and exposure characteristics. Five machine learning algorithms - logistic regression, support vector classifier, decision tree, random forest, and extreme gradient boosting - were employed to develop predictive models using a comprehensive dataset from existing studies.
We developed models using the initial dataset and a class weight approach to address data imbalance. For the imbalanced data, the Random Forest classifier outperformed others with 87% accuracy, 81% recall, and the fewest false negatives (23). In the class weight approach, the Support Vector Classifier minimized false negatives (21), while the Random Forest model achieved superior overall performance with 86% accuracy, 80% recall, and an F1-score of 82%. Furthermore, eXplainable Artificial Intelligence (XAI) techniques, specifically SHAP (SHapley Additive exPlanations) values, were utilized to quantify feature contributions to predictions, offering insights beyond traditional laboratory approaches. This study represents the first application of machine learning for predicting PM toxicity thresholds, providing a robust tool for health risk assessment.

The proposed methodology offers a time- and cost-effective alternative to classical laboratory tests, potentially revolutionizing PM toxicity threshold determination in scientific and epidemiological research. This innovative approach has significant implications for shaping regulatory policies and designing targeted interventions to mitigate health risks associated with airborne PM.
https://doi.org/10.1016/j.engappai.2024.109531

****

Debrauwer, L., Mervant, L., Laprevote, O., Jamin, E. L.
Pivotal Role of Mass Spectrometry for the Assessment of Exposure to Reactive Chemical Contaminants: From the Exposome to the Adductome.
Mass spectrometry reviews 2024; 1-20

A large part of the Human chemical exposome is now well characterized, and its health effects has been widely documented, although precise causal links remain difficult to establish. In parallel, genetic factors only were shown to contribute less than 30% to various pathologies. Therefore, environmental factors may represent the predominant cause of chronic diseases. Mass Spectrometry has been established for many years as a main "gold standard" in this field due to its performances both in sensitivity and selectivity. However, some unstable or highly reactive compounds may escape their detection in the biological samples because of their short half-life although some of their stable metabolites, if any, can be used for the exposure assessment. These electrophilic molecules are known to bind covalently to nucleophilic molecules in the body to form what are commonly called adducts. The study of adducts formed with DNA, proteins or with glutathione, nowadays called adductomics, can provide additional toxicologically relevant information in biomonitoring studies.
This review describes this particular part of the reactive exposome and the related mass spectrometric methods developed therein. Three dedicated parts of this review are devoted to the contribution of mass spectrometry respectively to the assessment of DNA modifications, protein modifications, and reaction with glutathione. © 2024 Wiley Periodicals LLC.
https://doi.org/10.1002/mas.21917

****

Delgado-Povedano, M. D. M., Maris, E., Kellner, N., Mulisa, G., Gámiz-Gracia, L., García-Campaña, A. M.*, et al.*
Liquid chromatography-tandem mass spectrometry for the determination of multiple mycotoxins in serum through suspect screening and targeted approaches: Advancing human mycotoxin biomonitoring.
Microchemical Journal 2025; Vol. 208 p 112562.

Human biomonitoring (HBM) is accepted as an effective way to assess human exposure to mycotoxins and to investigate their impact on human health. Ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) has emerged as a powerful tool for the quantitative and qualitative analysis of multiple mycotoxins in various matrices. However, there is a need for selective, sensitive and high-throughput methods using limited sample volumes. Here, the potential of suspect screening and targeted analysis by UHPLC-MS/MS for HBM of multiple mycotoxins in serum samples using an optimized sample pretreatment to ensure the highest coverage and the lowest limit of detection was investigated. A suspect screening method for 144 mycotoxins and metabolites using UHPLC-high-resolution MS/MS followed by data analysis using an in-house library was developed.
This library was incorporated into the UNIFI software and contained MS/MS information from the literature

as well as retention times determined experimentally (when commercial standards were available) or predicted using the retention time prediction Retip R package (when no commercial standards were available). The suspect screening and targeted methods were validated using pooled human serum spiked with 41 mycotoxins and metabolites standards and applied for HBM of multiple mycotoxins in serum samples from ten Ethiopian adults. In those ten samples, five different mycotoxins were detected using the suspect screening method, including ochratoxin B, for which no standard was available, while seven different mycotoxins were detected using the targeted method. The targeted method excelled in quantitative determination due to the lower limit of quantification for most mycotoxins. In contrast, the screening method, which does not require standards for qualitative analysis, may be particularly suitable for qualitative and semiquantitative determination of a large number of mycotoxins, including metabolites, in a large number of serum samples. In view of the complementarity of the two approaches, the developed suspect screening and targeted methods for mycotoxin analysis can be regarded as promising tools to better understand mycotoxin exposure and their metabolism in humans and address the associated health risks.
https://doi.org/10.1016/j.microc.2024.112562

****

Pili, S., Lecca, L. I., Pedrazzi, T., Ghitti, R., Murru, A., Uras, M.*, et al.*
Exposure assessment to fine and ultrafine particulate matter during welding activity in the maintenance shop of a steelmaking factory.
Heliyon 2024; Vol. 10 (23) p e40815.

Welding fumes are a main source of occupational exposure to particulate matter (PM), besides gases and ultraviolet radiations, that involves millions of operators worldwide and is related to several health effects, including lung cancer. Our study aims to evaluate the exposure to fine and ultrafine airborne particulate in welding operators working in a steel making factory.
In October 2019, air monitoring was performed for four days in five different welding scenarios and in the external area of a steelmaking factory to assess the exposure to airborne particles, ultrafine (UFP) particulate and inhalable fraction, during welding activities. The airborne particles distribution as particle number and mass concentration were measured using a low-pressure electric impactor, model ELPI (range of sampling 0.006mum and 10mum), whereas the airborne inhalable fraction was collected by filtration, using the IOM Sampler selector.The particle concentration, i.e. the number of particles per cm3 (part/cm3) showed significantly higher exposure figures for nanoscale particles, especially for the fractions included in the last 4 stages sampled by ELPI (from 0.010mum to 0.071mum), the figure representing between 85% and 91% of the total, whereas for the last 7 stages (0.010mum-0.314mum), they represented from 98% to 99% of the total. The average figure was approximately 5.01*104 part/cm3, while the maximum average was 1.95*105 part/cm3 on TIG welding, with a peak of 1.52*107 parts/cm3. In terms of mass concentration, the levels of PM inhalable fraction ranged between 0.1mg/m3 and 1.08mg/m3.
The results of the present study substantially confirm previous studies regarding the distributions in terms of number and mass of welding fumes for SMAW and TIG techniques on steel, the mass concentration levels resulting within the permissible exposure limits (PEL) indicated by OSHA regulations. The results highlighted the importance of the efficiency of localized aspiration systems and the need to apply prevention and protection measures despite the low levels of exposure measured in terms of mass.
Conclusion: Overall, The particle number concentrations showed an important contribution in the emission of UFP compared to background levels. The PM inhalable fraction was substantially contained within the PEL. Further studies are needed to better understand the chemical characterization of the particulate also considering further variables of the working process that could influence the levels of exposure to welding fumes.

https://doi.org/10.1016/j.heliyon.2024.e40815

****

Braun, G., Herberth, G., Krauss, M., Koenig, M., Wojtysiak, N., Zenclussen, A. C., Escher, B. I.
Neurotoxic mixture effects of chemicals extracted from blood of pregnant women.
Science 2024; Vol. 386 (6719)

Human biomonitoring studies typically capture only a small and unknown fraction of the entire chemical universe. We combined chemical analysis with a high-throughput in vitro assay for neurotoxicity to capture complex mixtures of organic chemicals in blood. Plasma samples of 624 pregnant women from the German LiNA cohort were extracted with a nonselective extraction method for organic chemicals. 294 of >1000 target analytes were detected and quantified. Many of the detected chemicals as well as the whole extracts interfered with neurite development. Experimental testing of simulated complex mixtures of detected chemicals in the neurotoxicity assay confirmed additive mixture effects at concentrations less than individual chemicals' effect thresholds.
The use of high-throughput target screening combined with bioassays has the potential to improve human biomonitoring and provide a new approach to including mixture effects in epidemiological studies.
https://doi.org/10.1126/science.adq0336

****

Hopf, N. B., Bessems, J., Santonen, T., Viegas, S., Casteleyn, L., Poddalgoda, D., *et al.*
Introducing the OECD guidance document on occupational biomonitoring: A harmonized methodology for deriving occupational biomonitoring levels (OBL).
Toxicology letters 2025; Vol. 403, p 132-143.

Derivation of occupational biomonitoring levels (OBLs) is needed to effectively utilize biomonitoring for assessing exposures to chemical substances, and consequently, implement risk reduction measures to reduce health risks among workers. OBLs are the appropriate option for chemical substances that can be absorbed through the skin. This methodology for derivation of OBLs has been developed in collaboration with scientific and regulatory experts from more than 40 institutes in 15 countries within the Organization for Economic Cooperation and Development (OECD) framework.
This manuscript provides a summary of the guidance on derivation of OBLs destined for scientists, risk assessors, and regulators who are tasked with establishing OBLs for regulatory purposes and implementing occupational biomonitoring programs. The derivation methodology follows a tiered approach based on the strength of evidence and quality of the data that we have labeled level of confidence. The tiered approach serves as a practical framework in occupational health risk assessment and management. We distinguish between four OBL levels depending on the strength of scientific evidence and confidence level: health-based derivation of OBL based on robust epidemiological data showing causal exposure-health effect relationship and Provisional OBL (POBL) based on robust toxicological animal data showing dose-response relationship as well as two assessment values which are not health based: reference levels in the general population (Reference OBL or (ROBL)), and Technical achievable OBL or (TOBL). Four case studies illustrating the derivation methods for OBLs and POBLs are also provided. Using this state-of-the-art approach (OECD guidance document no. 370) will lead to a harmonized derivation of OBLs and subsequently to evidence-based risk management measures.

https://doi.org/10.1016/j.toxlet.2024.12.006

****

Mahini, R. A., Casanola-Martin, G., Ludwig, S. A., Rasulev, B.
MixtureMetrics: A comprehensive package to develop additive numerical features to describe complex materials for machine learning modeling.
Softwarex 2024; Vol. 28 : 101911

Multi-component materials/compounds and polymeric/composite systems pose structural complexity that challenges the conventional methods of molecular representation in cheminformatics, which have limited applicability in such cases. Therefore, we have introduced an innovative structural representation technique tailored for complex materials. We implemented different mixing rules based on linear and nonlinear relationships' additive effect of different components in composites treating each multi-component material as a mixture system. We developed and improved mixture descriptors based on 12 different mixture functions grouped into three main categories: property-based descriptors, concentration-weighted descriptors, and deviationcombination descriptors. A python package was developed for this purpose, allowing users to compute 12 different mixture-descriptors to use as input for the generation of mixture-based Quantitative StructureActivity/Property Relationship (mxb-QSAR/QSPR) machine learning models for predicting a range of chemical and physical properties across various complex systems.
https://doi.org/10.1016/j.softx.2024.101911

****

Li, P., Zhu, B., Liu, Y., Huang, K., Fu, J., Zhang, H., *et al.*
Enhancing the Utilization of Nontarget Screening to Holistically Identify Chemical Exposure Fingerprints in Human Blood Biomonitoring and Epidemiological Study.
Environment & Health 2025;

Les humains sont exposés quotidiennement à divers produits chimiques synthétiques par diverses voies, notamment par l'alimentation, l'inhalation, le contact cutané et même par le cordon ombilical jusqu'au fœtus. De nombreux produits chimiques (p. ex., substances per- et polyfluoroalkylées, hydrocarbures aromatiques polycycliques, pesticides à base de triazine, stabilisants UV à base de benzotriazole, antioxydants phénoliques synthétiques) ont été définitivement documentés comme neurotoxiques pour le développement, perturbateurs endocriniens et cancérogènes. L'exposition aux produits chimiques est une cause importante de nombreuses maladies non transmissibles telles que le cancer, les fausses couches, les malformations congénitales, l'obésité, l'asthme, la pneumonie, le diabète sucré et la dépression. (1 à 3) Malgré les progrès réalisés dans l'exploration des associations entre certaines substances chimiques et les maladies, certaines questions scientifiques importantes restent en suspens, notamment l'identification des produits chimiques actuellement utilisés dans le commerce qui sont susceptibles de mettre en danger la santé humaine et l'estimation précise de la contribution de la pollution chimique à la maladie ou à la mort. (1) Par conséquent, l'identification complète des produits chimiques toxiques dans le corps humain est particulièrement préoccupante dans le monde entier, exacerbée par les tendances à l'augmentation rapide du nombre et de la production de produits chimiques.
https://doi.org/10.1021/envhealth.4c00256

****

Huang, J. L., Mao, J. Y., Liu, H. L., Li, Z. Y., Liang, G. Y., Zhang, D. B., *et al.*
Association between exposure to arsenic, cadmium, and lead and chronic kidney disease: evidence from four practical statistical models.

Environmental Geochemistry and Health 2025; Vol. 47 (1),p

Background Environmental exposure to arsenic (As), lead (Pb) and cadmium (Cd) may cause chronic kidney disease (CKD), with varying independent effects and unclear combined impact. This study aimed to evaluate these effects on CKD.
Methods : 1,398 individuals were included. Urine arsenic (UAs) was determined by atomic fluorescence method. Urinary cadmium (UCd) and blood lead (BPb) levels were determined by graphite-furnace atomic absorption spectrometry. CKD was defined as an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73m2 or proteinuria. Generalized linear models (GLM), restricted cubic spline (RCS) models, weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR) models were employed to study the independent and combined effects of exposure to As, Pb and Cd on CKD risk.
Results : Compared with non-CKD subjects, UAs, UCd, BPb, and creatinine adjusted urinary cadmium (UCdCr) were all significantly higher in CKD subjects. Compared with the lowest quartiles, the ORs (95%CIs) of CKD risk in the highest quartiles were 2.09 (1.16-3.74) for UAs, 2.84(1.56-5.18) for UCd, and 1.79 (1.05-3.06) for UCdCr, respectively. UAs, UCd, and UCdCr were all significantly positively associated with CKD risk in p-trend tests. RCS models revealed non-linear links between UAs, UCd, UCdCr and CKD risk, while a linear dose-response existed for BPb and CKD risk. The OR (95%CI) in WQS models were 1.72 (1.25-2.36) with UAs being the highest weighing metal(loid). BKMR models showed co-exposure mixture linked to higher CKD risk when the ln-transformed metal(loid)s above their 55th percentile. The ln-transformed UAs and UCdCr was significantly positively associated with CKD risk when the other two ln-transformed metals levels were all fixed at their different percentile levels. Synergism between Cd and Pb was also apparent.
Conclusions : Single As, and Cd exposure were positively associated with an increased CKD risk. Co-exposure to As, Pb and Cd was positively associated with CKD risk, with As playing a dominant role.
https://doi.org/10.1007/s10653-024-02318-3

****

Batlle, J. V. I.
Modelling the combined effects of ionising radiation and chemical pollutants on wildlife populations.
Journal of Environmental Radioactivity 2025; Vol. 282,p

A population model is presented to study the combined effects of ionising radiation and chemical pollutants on wildlife. The model is based on first order, non-linear and logistic differential equations combining mortality, morbidity and reproduction phenomena with life history data and ecological interactions. Acclimation is considered as a possible mechanism to study theoretically this effect at low levels of radiation or chemical concentration. Radiation and chemical-induced damages are represented by a 'repairing pool' mediating between healthy, damaged, acclimated, and irrecoverable individuals. Damages to population, fecundity and the repairing pool are represented by a linear-quadratic function combining radiation dose and chemical concentration terms. The endpoints of the model are repairable damages (morbidity), impairment of reproductive ability and mortality. The model is evaluated with a mixed ionising radiation/arsenate demonstration scenario to illustrate the combined effect of radiation and chemical pollutants upon the sustainability of a hypothetical vole population, including the influence of acclimation, given the assumption that the repair of both radiation and toxicity damages share the same mechanism. A sensitivity analysis of the model illustrates the effects of combining radiation dose and chemical concentration on self-repairing and reproductive ability for the population, exploring cases of antagonism and synergism by varying the relevant model parameters. This model provides a conceptual framework to address mixed radiological and chemical effects to wildlife populations. It can be used to assess the robustness of the benchmarks used in wildlife radiological assessment, informing ongoing regulatory debates on their applicability to mixed stressor situations. Future research will enable to draw conclusions

about the most restrictive mixed exposure situations in terms of effects to the population.
https://doi.org/10.1016/j.jenvrad.2025.107615

****

- ## Co-expositions aux métaux lourds

Tabassum, B.
Editorial: E-waste and heavy metals: health hazards and environmental impact.
Frontiers in Public Health 2024; Vol. 12,p

As the topic editor for "E-Waste and Heavy Metals: Health Hazards and Environmental Impact," I am honored to present a Research Topic that addresses the urgent global challenge of e-waste management and the health risks posed by heavy metals. In an era of rapid technological growth, e-waste has become a critical environmental concern, threatening both ecosystems and human health due to hazardous metals like lead, mercury, cadmium, and nickel.
This Research Topic integrates diverse studies that analyse the health consequences of heavy metals from a variety of perspectives. A cross-sectional study on the association between anxiety and blood cadmium, lead, and mercury is a notable manuscript that provides valuable perspectives into the neurotoxic effects of heavy metal exposure. Investigations on systemic inflammation due to combined heavy metals and the risk of metabolic disorders like metabolic syndrome and fatty liver disease are equally significant.
https://doi.org/10.3389/fpubh.2024.1506438

****

Fu, Z., Xu, X., Cao, L., Xiang, Q., Gao, Q., Duan, H.*, et al.*
Single and joint exposure of Pb, Cd, Hg, Se, Cu, and Zn were associated with cognitive function of older adults.
Scientific Reports 2024; Vol. 14 (1) p 28567.

Background: Impaired cognitive function following exposure to heavy metals has emerged as a significant global health concern. Nevertheless, the impact of combined exposure to multiple heavy metals on cognitive impairment remains unclear.
Objective: This study aimed to explore the association between multiple heavy metals exposure and cognitive function to provide theoretical evidence to guide prevention strategies.
Methods: The blood levels of lead (Pb), cadmium (Cd), mercury (Hg), selenium (Se), copper (Cu) and zinc (Zn) and the results of the cognitive function tests were extracted from 811 elderly Americans who completed the NHANES between 2011 and 2014. Quantile regression (QR), restricted cubic splines (RCS), and Bayesian kernel machine regression (BKMR) were used to explore the individual and joint association between heavy metals exposure and performance in 4 standardized cognitive tests; Item Response Theory (IRT), Delayed Recall Test (DRT), Animal Fluency Test (AFT) and Digit Symbol Substitution Test (DSST).
Results: A negative association was noted between Cd levels and IRT ($p = 0.048$, 95%CI: -2.7, -0.1). Se concentrations ranging between 2.197 µg/L (95%CI: 0.004, 0.15) to 2.29 µg/L (95%CI: 2.56, 7.64) (log10Se) was postively associated with DSST ($p = 0.001$). Cu was negatively associated with DSST ($p = 0.049$, 95%CI: -37.75, -0.09), while Zn was positively associated with IRT ($p = 0.022$, 95%CI: 0.55, 11.73). Exposure to the 6 heavy metals combined showed a positive linear association with IRT, DRT, and a negative linear association with DSST. An interaction between Cd and the other heavy metals (excepted for Pb).

Conclusion: Exposure to Pb, Cd, Hg, Se, Cu, and Zn was associated with cognitive function. Joint exposure to the 6 heavy metals showed a positive linear association with IRT, DRT, contrarily, a negative linear association with DSST.
https://doi.org/10.1038/s41598-024-79720-5

****

Wang, T., Xue, L., Li, C., Zhao, D., Huan, J., Han, X.*, et al.*
The interaction between plasma polymetals and lifestyle on cognitive dysfunction in occupational aluminum exposed workers: A cross-sectional study in China.
NeuroToxicology 2024; Vol. 105, p 313-322.

Objective : To investigate the interaction between plasma polymetallic exposure and lifestyle factors on cognitive function abnormalities in occupational aluminum workers. The aim is to develop a new occupational health management model that integrates lifestyle behaviors with occupational activities to comprehensively protect the health of these workers.
Method : 476 Participants were recruited from an aluminum factory in Shanxi, China. Cognitive functioning was assessed using the Montreal Cognitive Assessment Scale (MoCA). Plasma polymetallic levels were measured using ICP-MS. Logistic regression analyzed the relationship between nine plasma metals, lifestyle factors, and cognitive abnormalities. A 3D model validated the interaction between metals and analyzed the combined effects of plasma metals and lifestyle on MoCA scores. The Chi-squared Automatic Interaction Detector (CHAID) decision tree was used to identify factors influencing cognitive dysfunction.
Results : High blood aluminum concentration (>47.85 µg/L), high blood lithium concentration (>3.15 µg/L), as well as sleep time (≤7 h and > 8 h), smoking, alcohol consumption, and length of mobile phone use(≥2 h) were risk factors for abnormal cognitive functioning. In addition aluminum and lithium have a multiplicative interaction on cognitive function (OR=1.86,95 %CI:1.14,3.050). There was an interaction between high plasma levels of aluminum and lithium and smoking on cognitive function in workers, and an interaction between high plasma levels of aluminum and lithium and sleep duration ≤7 or >8 h on cognitive function in workers.
Conclusion : The levels of blood metal elements aluminum and lithium, as well as sleep time, smoking, drinking, and length of mobile phone use, are risk factors for cognitive dysfunction in occupational aluminum workers. There are the synergetic effect to increase the risk of cognitive dysfunction between blood aluminum concentration ≥50.59µg/L and blood lithium concentration ≥3.44µg/L, sleep duration ≤7h& >8 h, smoking, drinking, mobile phone use ≥2 h.
https://doi.org/10.1016/j.neuro.2024.11.002

****

Lu, O. Y., Li, Q., Yang, S., Yan, L. Y., Li, J. J., Wan, X.*, et al.*
Interplay and long-lasting effects of maternal low-level Pb, Hg, and Cd exposures on offspring cognition.
Ecotoxicology and Environmental Safety 2024; Vol. 287 : 117315

Lead (Pb), mercury (Hg), and cadmium (Cd) are prevalent and persistent environmental contaminants, causing detrimental effects on millions of individuals worldwide. Our previous research demonstrated that early-life exposure to low-level Pb, Hg, and Cd mixtures may lead to cognitive impairments. However, the association and interaction among low levels of Pb, Hg, or Cd exposure remains unclear.
In this study, a two-level full factorial design (5.481, 0.036, and 2.132 mg/L for Pb, Hg, and Cd respectively) was conducted to assess the interplay among maternal Pb, Hg, and Cd exposure on offspring cognition. Following exposure during pregnancy and lactation, a competitive absorption among Pb, Hg, and Cd was

observed. Maternal exposure to each metal alone resulted in higher blood and brain concentrations of Pb, Hg, and Cd in offspring compared to co-exposure at equivalent levels. However, behavioral experiments conducted in the Morris water maze and novel object recognition test revealed maternal Pb, Hg, and Cd exposure synergistically impaired offspring's spatial cognition and recognition memory. Importantly, this dysfunction persisted into middle age even without exposure after adulthood.
Moreover, the open field test and elevated plus maze indicated maternal low-level Pb, Hg, and Cd coexposure triggered risk-taking behavior in weaning offspring, with a significant main effect for Pb exposure. No long-lasting effect on risk-taking behavior was detected in middle-aged offspring. Further investigation into molecular mechanisms showed that the dysregulation of corticosterone reaction and immune response might be the potential mechanism underlying Pb, Hg, and Cd co-exposure-induced cognitive impairments.
Our study highlights the synergistic and long-lasting effects of multiple heavy metal exposures, underscoring the urgency to prevent exposure to metal mixtures among children and women of childbearing age.
https://doi.org/10.1016/j.ecoenv.2024.117315

****

Wei, M.-H., Li, J.-X., Mi, J., Wang, Q., Xu, F., Xu, C.
Associations between co-exposure to multiple heavy metals and age-related macular degeneration: A cross-sectional study.
Journal of Trace Elements in Medicine and Biology 2025; Vol. 87, p 127573.

Background & aims : Accumulating evidence suggests that exposure to single heavy metal can facilitate the progression of age-related macular degeneration (AMD). However, the effects of exposure to mixtures of heavy metals on AMD remain largely unexplored. This study aims to investigate both the joint and individual impacts of arsenic (As), mercury (Hg), cadmium (Cd), and lead (Pb) on AMD within a co-exposure framework.
Methods Data from subjects participating the US National Health and Nutrition Examination Survey (NHANES, 2005–2008) were analyzed. Concentrations of As, Hg, Cd, and Pb were determined in urine by inductively coupled plasma dynamic reaction cell mass spectrometry (ICP-DRC-MS) for As and Hg, and inductively coupled plasma mass spectrometry (ICP-MS) for Cd and Pb. The weighted quantile sum (WQS) and Bayesian kernel machine regression (BKMR) models were employed to assess the effects of heavy metal mixtures on AMD risk.
Results Both WQS and BKMR analyses consistently revealed a significant overall association between heavy metal mixtures and the risk of all types of AMD. The combined effect was more evident among patients with early AMD compared to those with late AMD. Cd and Hg were the main contributors driving these combined effects within the context of metal mixtures. Elevated urinary levels of Cd were positively correlated with an increased risk for all types as well as early AMD. Higher exposure to Hg corresponded with an elevated risk for early AMD. Furthermore, BKMR analysis indicated that the influence of Cd on early AMD exhibited a non-linear pattern.
Conclusions Our findings suggest that co-exposure to As, Hg, Cd, and Pb is associated with an elevated risk for developing AMD, particularly in its early stages. Furthermore, excessive exposure to Cd and Hg has been identified as key contributing factors in this process.
https://doi.org/10.1016/j.jtemb.2024.127573

****

Long, C., Wang, X., Wang, D., Chen, Y., Zhang, B.

Deciphering the impact of heavy metal mixed exposure on lipid metabolism using three statistical models.
Environmental geochemistry and health 2024; Vol. 47 (1) p 20.

Lipid metabolism disorders pose a significant threat to human health. However, the relationship between heavy metal mixed exposure and lipid metabolism remains poorly understood. This study recruited 1717 residents living near a chromium factory in northeast China. The concentrations of blood Cr, Mn, Cd, Pb, V, and serum CHOL, TG, LDL and HDL levels were measured. Generalized linear model (GLM), quantile g-computation (Qg-comp), and Bayesian kernel machine regression (BKMR) were simultaneously employed to investigate the associations between heavy metal mixed exposure and lipid markers levels.
GLM analysis revealed significant associations between blood Cr concentration and HDL (beta=-0.07; 95%CI: -0.09, -0.05), LDL (beta=-0.06; 95%CI: -0.11, -0.02), and CHOL (beta=0.07; 95%CI: 0.01, 0.12) levels. V concentration was positively associated with HDL (beta=0.12; 95%CI: 0.06, 0.18) and LDL (beta=0.17; 95%CI: 0.04, 0.30) levels. Qg-comp analysis indicated a negative association between heavy metal mixed exposure and HDL (beta=-0.040; 95%CI: -0.073, -0.006) level. BKMR model further confirmed the negative relationship between heavy metal mixed exposure and HDL, with the interaction between blood Cr (>1.05mug/L) and blood V (>5.16mug/L) contributing to decreased HDL levels.
Our findings suggested that heavy metal mixed exposure had impacts on HDL and CHOL levels, and the Cr and V may mutually play a predominant role in the observed abnormal HDL levels.

https://doi.org/10.1007/s10653-024-02328-1

****

Wu, H., Feng, L., Wu, H., Wang, L., Xu, H., Fu, F.
Synergistic effects of PS-NPs and Cd on ovarian toxicity in adolescent rats: Ferroptosis by induction of mitochondrial redox imbalance via the SIRT3-SOD2/Gpx4 pathway.
Ecotoxicology and Environmental Safety 2025; Vol. 290, p 117622.

Nanoplastics (NPs) are an emerging class of pollutants. They can act as a“Trojan horse” to change the bioavailability and toxicity of heavy metals in the environment. However, research on the combined toxicity of heavy metals and NPs is scarce, especially during the critical developmental period of adolescence. In this study, polystyrene nanoplastics (PS-NPs) and/or cadmium (Cd) were exposed to 4-week-old female rats for 28 days, with the aim of exploring the potential effects of combined exposure to PS-NPs and Cd on the ovaries of adolescence rats.
Results showed that co-exposure to PS-NPs and Cd exacerbated ovarian toxicity in rats, primarily through increased atretic follicle numbers and endocrine disruption. Further studies revealed that PS-NPs and Cd synergistically repressed the SIRT3-SOD2/Gpx4 pathway, inducing mitochondrial oxidative stress and ferroptosis, resulting in damage to ovarian structure and function. However, the addition of the mitochondrion-targeted antioxidant SS-31 and the ferroptosis inhibitor Fer-1 reversed the harm to the ovaries from co-exposure to PS-NPs and Cd, the aberrant expression of genes related to the SIRT3-SOD2/Gpx4 pathway was also improved. Our results suggested that co-exposure to PS-NPs and Cd may trigger ferroptosis by inhibiting the SIRT3-SOD2/Gpx4 pathway, leading to mitochondrial redox imbalance, which provided novel insights into reproductive toxicity due to the interaction of PS-NPs and Cd during adolescence.
https://doi.org/10.1016/j.ecoenv.2024.117622

****

Chen, J., Chen, J., Li, M., Feng, P., Qin, M., Chen, T.*, et al.*
Probabilistic assessment of the cumulative risk from dietary heavy metal exposure in Chongqing, China using a hazard-driven approach.
Scientific reports 2025; Vol. 15 (1),p 2229.

Cumulative risk assessment is significant for evaluating the combined exposure to multiple substances, but its widespread acceptance and application have been limited due to the complexity of clarifying and assessing actual exposure. In this study, we conducted a cumulative risk assessment based on hazard-driven criteria to evaluate the co-exposure to elemental contaminants in the diet of the population in Chongqing Municipality. The cumulative risk was calculated and evaluated using Monte Carlo modeling and the modified Reference Point Index (mRPI) method. Neurotoxicity and nephrotoxicity were identified as the main toxic endpoints, and the final evaluation elements included were Pb, Cd, As, and Hg.
The results showed that the combined mRPI values for neurotoxicity and nephrotoxicity, resulting from exposure to the four heavy metals, ranged from 0.922 to 4.835 and 1.306 to 7.031, respectively. Cd and Pb were the primary contributors to nephrotoxicity, while Pb was the main contributor to neurotoxicity. The results indicated that combined dietary exposure to Pb, Cd, As, and Hg may pose risks of neurotoxicity and nephrotoxicity, with the combined exposure likely amplifying this risk compared to exposure to individual heavy metal elements. mRPI proves to be a more suitable index for cumulative risk assessment using a hazard-driven approach compared to other indexes, as it is derived based on specific studies and endpoints.

https://doi.org/10.1038/s41598-024-83299-2

****

Sun, Z. H., Xu, Y., Liu, Y., Tao, X. Y., Zhou, P., Feng, H.*, et al.*
Associations of Exposure to 56 Serum Trace Elements with the Prevalence and Severity of Acute Myocardial Infarction: Omics, Mixture, and Mediation Analysis.
Biological Trace Element Research 2025; Vol.

Several studies have reported associations between specific heavy metals and essential trace elements and acute myocardial infarction (AMI). However, there is limited understanding of the relationships between trace elements and AMI in real-life co-exposure scenarios, where multiple elements may interact simultaneously. This cross-sectional study measured serum levels of 56 trace elements using inductively coupled plasma mass spectrometry. We identified individual trace elements linked to AMI using four feature selection methods and evaluated their associations with AMI prevalence and severity through multiple-element logistic regression. Restricted cubic spline analysis was employed to examine non-linear associations. Additionally, we explored the associations between trace element mixtures and AMI prevalence and severity using Bayesian kernel machine regression (BKMR) and element risk score (ERS). Finally, we investigated the potential mechanisms linking trace element exposure to AMI. We detected stable positive associations and linear relationships between Cu and Rb and AMI prevalence and severity. Furthermore, lower Fe concentrations were associated with higher AMI prevalence, while higher Sb concentrations were linked to greater AMI severity. Both BKMR and ERS models indicated positive associations between trace element mixtures and AMI prevalence and severity. Mediation analysis suggested that high-sensitivity C-reactive protein partially mediated the associations between trace elements and AMI prevalence and severity.
We provide the first epidemiological evidence of the associations between serum trace element mixtures and AMI prevalence and severity. Under conditions of trace element co-exposure, Cu, Rb, Fe, and Sb were

closely associated with AMI. Additionally, our results indicate that hsCRP (inflammation) may be a potential mechanism linking trace elements to AMI.
https://doi.org/10.1007/s12011-024-04509-6

****

Cheng, T., Yu, D., Li, G., Chen, X., Zhou, L., Wen, Z.
Association between exposure to urinary metal and all-cause and cardiovascular mortality in US adults.
PloS one 2024; Vol. 19 (12),p e0316045.

BACKGROUND: Further evidence is required regarding the influence of metal mixture exposure on mortality. Therefore, we employed diverse statistical models to evaluate the associations between eight urinary metals and the risks of all-cause and cardiovascular mortality.;
METHODS: We measured the levels of 8 metals in the urine of adults who participated in the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2018. Based on follow-up data, we determined whether they died and the reasons for their deaths. We estimated the association between urine metal exposure and all-cause mortality using Cox regression, weighted quantile sum (WQS) regression, and Bayesian kernel machine regression (BKMR) models. Additionally, we used a competing risk model to estimate the relationship between metal exposure and cardiovascular mortality.;
RESULTS: Among the 14,305 individuals included in our final analysis, there were 2,066 deaths, with 1,429 being cardiovascular-related. Cox regression analysis showed that cobalt (Co) (HR: 1.21; 95% CI: 1.13, 1.30) and antimony (Sb) (HR: 1.26; 95% CI: 1.12, 1.40) were positively associated with all-cause mortality (all P for trend <0.001). In the competing risk model, Co (HR: 1.29; 95% CI: 1.12, 1.48), lead (Pb) (HR: 1.18; 95% CI: 1.03, 1.37), and Sb (HR: 1.44; 95% CI: 1.18, 1.75) were significantly associated with an increased risk of cardiovascular mortality (all P for trend <0.001). Sb, Pb, cadmium (Cd), and molybdenum (Mo) had the highest weight rankings in the final WQS model. All metals showed a complex non-linear relationship with all-cause mortality, with high posterior inclusion probabilities (PIPs) in the final BKMR models.;
CONCLUSIONS: Combining all models, it is possible that Sb may have a more stable impact on all-cause and cardiovascular mortality. Meaningful metal effects in individual statistical models still require careful attention.

https://doi.org/10.1371/journal.pone.0316045

****

- ## Multiexpositions aux Pesticides, VOCs, polluants

Gois, M. F. B., Fernandez-Pato, A., Huss, A., Gacesa, R., Wijmenga, C., Weersma, R. K.*, et al.*
Impact of occupational pesticide exposure on the human gut microbiome.
Frontiers in Microbiology 2023; Vol. 14

The rising use of pesticides in modern agriculture has led to a shift in disease burden in which exposure to these chemicals plays an increasingly important role. The human gut microbiome, which is partially responsible for the biotransformation of xenobiotics, is also known to promote biotransformation of environmental pollutants. Understanding the effects of occupational pesticide exposure on the gut

microbiome can thus provide valuable insights into the mechanisms underlying the impact of pesticide exposure on health.
Here we investigate the impact of occupational pesticide exposure on human gut microbiome composition in 7198 participants from the Dutch Microbiome Project of the Lifelines Study. We used job-exposure matrices in combination with occupational codes to retrieve categorical and cumulative estimates of occupational exposures to general pesticides, herbicides, insecticides and fungicides. Approximately 4% of our cohort was occupationally exposed to at least one class of pesticides, with predominant exposure to multiple pesticide classes. Most participants reported long-term employment, suggesting a cumulative profile of exposure. We demonstrate that contact with insecticides, fungicides and a general "all pesticides" class was consistently associated with changes in the gut microbiome, showing significant associations with decreased alpha diversity and a differing beta diversity.
We also report changes in the abundance of 39 different bacterial taxa upon exposure to the different pesticide classes included in this study. Together, the extent of statistically relevant associations between gut microbial changes and pesticide exposure in our findings highlights the impact of these compounds on the human gut microbiome.
https://doi.org/10.3389/fmicb.2023.1223120

****

Wang, F., Lin, Y., Qin, L., Zeng, X., Jiang, H., Liang, Y.*, et al.*
Serum metabolome associated with novel and legacy per- and polyfluoroalkyl substances exposure and thyroid cancer risk: A multi-module integrated analysis based on machine learning.
Environment international 2024; Vol. 195, p 109203.

BACKGROUND: Exposure to per- and polyfluoroalkyl substances (PFAS) may linked to thyroid cancer (TC) risk, but inconsistent findings and a lack of studies on mixed exposures exist, especially regarding novel PFAS compounds. Additionally, little is known about the potential mechanisms underlying the association.;
OBJECTIVES: Explore the effects of PFAS exposure on the serum metabolome and its correlation with TC.;
METHODS: A 1:1 age- and sex-matched case-control study was administered with 746 TC cases and healthy controls. Liquid chromatography-high resolution mass spectrometry determined serum 11 PFAS and untargeted metabolome profile. ENET and LightGBM models were used to explore the exposure patterns and perform variable selection. The mixed exposure effects were assessed using Weighted quantile sum regression and Bayesian kernel machine regression. Metabolome-wide association analyses were performed to assess metabolic dysregulation associated with PFAS, and a structural synthesis analysis was used to detect latent groups of individuals with TC based on PFAS levels and metabolite patterns.;
RESULTS: Ten of the 11 PFAS were detected in>80% of the population. PFHxA and PFDoA exposure associated with increased TC risk, while PFHxS and PFOA associated with decreased TC risk in single compound models (all $P < 0.05$). Machine learning algorithms identified PFHxA, PFDoA, PFHxS, PFOA, and PFHpA as the key PFAS influencing the development of TC, and mixed exposures have an overall positive effect on TC risk, with PFHxA making the primary contribution. A novel integrative analysis identified a cluster of TC patients characterized by increased PFHxA, PFDoA, PFHpA and decreased PFOA, PFHxS levels, and altered metabolite patterns highlighted by the upregulation of free fatty acids.;
CONCLUSIONS: PFAS exposure is linked to a higher risk of TC, possibly through changes in fatty acid metabolism. Larger, prospective studies are needed to confirm these findings, and the role of short-chain PFAS requires more attention.

https://doi.org/10.1016/j.envint.2024.109203

****

Shao, W., Gong, P., Wang, Q., Ding, F., Shen, W., Zhang, H.*, et al.*

Association of exposure to multiple volatile organic compounds with ultrasound-defined hepatic steatosis and fibrosis in the adult US population: NHANES 2017–2020.

Frontiers in Public Health 2025; Vol. 12

Objective: Volatile organic compounds (VOCs) are pervasive environmental pollutants known to impact human health, but their role in liver steatosis or fibrosis is not fully understood. This study investigates the association of urinary VOC mixtures with the risk of liver steatosis and fibrosis in U.S. adult population.
Methods: Data of 1854 adults from the National Health and Nutrition Examination Survey (NHANES) from 2017.01 to 2020.03 were collected. Vibration Controlled Transient Elastography (VCTE) assessed hepatic steatosis and liver fibrosis via the controlled attenuation parameter (CAP) and liver stiffness measurement (LSM), respectively. The study examined the relationship between urinary exposure biomarkers for 20 VOCs and liver health outcomes using multivariate logistic regression and Bayesian Kernel Machine Regression (BKMR) to evaluate the effects of both individual and mixed VOC exposures.
Results: Multivariate logistic regression analysis revealed that exposure biomarkers for acrolein and crotonaldehyde were positively associated with hepatic steatosis. Conversely, biomarkers for styrene, ethylbenzene, and propylene oxide were negatively associated with hepatic steatosis. Furthermore, biomarkers for 1,3-butadiene and xylene were positively associated with liver fibrosis, while ethylbenzene was negatively associated with this condition. BKMR analysis identified a significant positive joint effect of VOC biomarkers on CAP. Notably, when other VOC-EBs were held at median levels, biomarkers for acrolein and 1,3-butadiene exhibited linear correlations with Ln CAP and hepatic Ln LSM, respectively.
Conclusion: The study highlights the potential hepatotoxic effects of VOC mixtures, particularly noting the roles of acrolein and 1,3-butadiene in exacerbating liver steatosis and fibrosis. These findings advocate for further research to explore the mechanistic pathways and conduct longitudinal studies to establish causality and enhance understanding of VOCs' impact on liver health.
https://doi.org/10.3389/fpubh.2024.1437519

****

Wesley, S. R., Gallo, M., Apata, T., Dis, J. V., Hollenbach, S. J.

Impact of Endocrine-Disrupting Chemicals, Climate, and Air Pollution on Pregnancy Outcomes: A Scoping Review.

Semin Reprod Med 2024; Vol. (eFirst),p

Environmental pollutants, including endocrine-disrupting chemicals (EDCs), air pollution, and climate change, are increasingly recognized for their potential impact on pregnancy outcomes. EDCs, found in pesticides, industrial chemicals, and personal care products, are associated with preterm birth and fetal growth restriction, primarily through hormonal interference. Air pollution, notably PM2.5, NO2, and O3, has been linked to increased rates of preterm birth, low birth weight, and stillbirth. Climate factors, such as extreme heat, elevate risks of pregnancy loss and preterm birth, with significant impacts on vulnerable populations across diverse socioeconomic and geographic regions. These exposures contribute to adverse pregnancy outcomes through mechanisms involving oxidative stress, inflammation, and endocrine disruption. The interplay among these environmental factors underscores the need for integrated, longitudinal studies to understand their combined effects on pregnancy outcomes better. Future research should focus on region-specific impacts, cumulative exposure, and policy-driven interventions to mitigate these environmental risks, especially in vulnerable populations disproportionately affected by these hazards. This scoping review synthesizes recent findings from 2019 to 2024 to highlight these associations

and identify research gaps.
https://doi.org/10.1055/s-0044-1800961

****

Wu, X., Wei, D., Zhou, Y., Cao, Q., Han, G., Han, E., *et al.*
Pesticide exposures and 10-year atherosclerotic cardiovascular disease risk: Integrated epidemiological and bioinformatics analysis.
Journal of Hazardous Materials 2025; Vol. 485, p 136835.

Background and purpose Recent studies link pesticide exposures to cardiovascular disease risk factors. However, research on the combined effects of multiple pesticides on atherosclerotic cardiovascular disease (ASCVD) is limited, particularly in rural areas. Despite advances in toxicogenomics, the mechanisms underlying these effects remain unclear. This study aims to investigate the combined effects and mechanisms of pesticide exposures on ASCVD.
Methods In the cross-sectional study section, 2291 participants were included. Variables were filtered using machine learning models, and associations between mixed exposure to multiple pesticides and ASCVD were explored using environmental mixed exposure models (weighted quartile sum (WQS) regression and quantile-based g-computation (QGC)). In the bioinformatics analysis section, the GEO, CTD, Malacards, and GeneCards databases were used to retrieve target genes for pesticide exposure and atherosclerotic diseases. Enrichment analysis was then performed to identify the biological pathways associated with these genes.
Results Three machine models screened 34 pesticides. Single pesticide exposures, such as atrazine, oxadiazon, p,p'-DDE, α-BHC, β-BHC, fenitrothion, malathion, fenitrothion, cypermethrin, cypermethrin, and cypermethrin might increase the 10-year ASCVD risk (all $P < 0.05$). Total mixed pesticide exposure was positively associated with 10-year ASCVD risk in both the QGC (3.223(2.196, 4.730)) and WQS models (4.642(3.070, 7.020)). Notably, there was a linear relationship between totalQGC ($P\_overal < 0.001$; $P\_nonlinearity = 0.864$) and high 10-year ASCVD risk. In toxicogenomic bioinformatics analysis, we identified 112 potential atherosclerosis target genes affected by pesticide exposure. Pathway enrichment analysis suggests pesticide-induced atherosclerosis is linked to pathways such as metabolic pathways, lipid metabolism, MAPK, AMPK, FoxO signaling, apoptosis, fluid shear stress, endocrine resistance, TNF, and PI3K-Akt. Key genes were identified based on maximal clique centrality, including AKT1, TP53, IL6, BCL2, TNF, JUN, PTGS2, CASP3, MAPK3, and CASP9.
Conclusion Individual and combined exposure to pesticides increased the 10-year ASCVD risk, especially in patients with T2DM. Mixed levels of pesticide exposure were linearly and positively associated with high 10-year ASCVD risk. The mechanism of atherogenesis by mixed pesticide exposure may involve pathways such as lipid metabolism, MAPK, AMPK, FoxO signaling, apoptosis, fluid shear stress, endocrine resistance, TNF, and PI3K-Akt.
https://doi.org/10.1016/j.jhazmat.2024.136835

****

Bian, J., Guo, Z., Liao, G., Wang, F., Yu, Y. H. K., Arrandale, V. H., *et al.*
Increased health risk from co-exposure to polycyclic aromatic hydrocarbons, phthalates, and per- and polyfluoroalkyl substances: Epidemiological insight from e-waste workers in Hong Kong.
The Science of the total environment 2025; Vol. 958 p 177912.

The alarming surge in electronic waste (e-waste) in Hong Kong has heightened concerns regarding occupational exposure to a myriad of pollutants. Among these, polycyclic aromatic hydrocarbons (PAHs),

phthalates (PAEs), and per- and polyfluoroalkyl substances (PFASs) are prevalent and known for their harmful effects, including the induction of oxidative stress and DNA damage, thereby contributing to various diseases. This study addresses gaps in knowledge by investigating exposure levels of these pollutants-measured via hydroxylated PAHs (OH-PAHs), phthalate metabolites (mPAEs), and PFASs-in urine from 101 e-waste workers and 100 office workers. E-waste workers exhibited higher concentrations of these substances compared to office workers. Elevated urinary levels of OH-PAHs, mPAEs, and PFASs correlated significantly with increased 8-hydroxy-2-deoxyguanosine (8-OHdG) levels (beta=2.53, 95% CI: 2.12-3.02).
The association between short-chain PFASs (Perfluoropentanoic acid, PFPeA) and DNA damage was discovered for the first time. Despite most participants (95%) showing hazard index (HI) values below non-carcinogenic risk thresholds for PAHs and PAEs, certain pollutants posed higher risks among e-waste workers, necessitating enhanced protective measures.
Moreover, the 95th percentile of carcinogenic risk associated with diethylhexyl phthalate (DEHP) exceeded 10-4 in both groups, highlighting the urgent need for regulatory measures to mitigate DEHP exposure risks in Hong Kong.

https://doi.org/10.1016/j.scitotenv.2024.177912

****

Song, X., Zhu, X., Liu, X., Wang, Z., Kou, Z., Liu, W.*, et al.*
Association of Organophosphorus Pesticide and Glyphosate Exposure with Nasal Flora and Total IgE in Solar Greenhouse Workers: A Unique Farmer Group.
Environmental pollution (Barking, Essex : 1987) 2025; Vol. p 125698.

Studies have shown that the presence of allergens, including insecticides, significantly increases the risk of occupational allergic diseases among solar greenhouse workers. However, no studies have yet investigated the relationship between organophosphorus pesticide use by greenhouse workers and allergic diseases, and the role of the flora in this context remains unclear.
Therefore, this study aimed to investigate the relationship between combined exposure to organophosphorus pesticides (OPs) and Glyphosate (GLY) and changes in total immunoglobulin E (IgE) levels, as well as to analyze the role of nasal flora in allergic status. We collected demographic data, urine, peripheral blood and nasal swab samples from 284 solar greenhouse workers.
Six metabolites in urine were detected by ultra-high-performance liquid chromatography coupled with tandem mass spectrometry (UPLC-MS/MS). Total IgE concentration was determined by enzyme-linked immunosorbent assay (ELISA). We then evaluated the association between OPs and GLY with total IgE levels using logistic regression analysis. In addition, 66 participants received 16S rDNA sequencing of nasal flora, followed by community diversity and species difference analyses to identify distinct microbial communities between normal and abnormal total IgE groups. A total of 284 participants were included in this study, of whom 132 (46.5%) and 152 (53.5%) were male and female, respectively. The median total IgE concentration in this population was 63.52 IU/mL, of which 89 (31.3%) belonged to the elevated total IgE group. Our results suggest that dimethylphosphorodithioate (DMDTP) was a risk factor for total IgE abnormality, and glyphosate (GLY) was positively associated with total IgE abnormality. Additionally, 20 differential flora were identified between the elevated and normal IgE groups, of which at least 7 were significantly associated with OPs, GLY and its metabolites.
In conclusion, there was a positive correlation between exposure to OPs and GLY and total IgE abnormalities, as well as multiple nasal pathogenic flora.
https://doi.org/10.1016/j.envpol.2025.125698

****