Bulletin de veille Perturbateurs Endocriniens N°25 - Mai – Juin 2024

Objectif : cette veille bibliographique à pour objectif la surveillance de l'actualité et de la littérature scientifique sur les perturbateurs endocriniens. Cette veille est axée sur les aspects suivants : l'exposition, la toxicité, l'évaluation, la prévention, l'épidémiologie et l'actualité.

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 liens mentionnés dans le bulletin donnent accès aux documents sous réserve d'un abonnement à la ressource.

Exposition professionnelle

Effect of occupational exposure to vat-textile dyes on follicular and luteal hormones in female dye workers in Abeokuta, Nigeria.

Soyinka OO, Akinsanya AF, Odeyemi FA, Amballi AA, Oritogun KS, Ogundahunsi OA. *Afr Health Sci*. 2024 2024 Apr 01;24(1):135-44.

Background: Some synthetic dyes used mainly in textile industries have been associated with endocrine disruption, resulting in infertility, among other disorders. It is unknown if occupational exposure to Vat textile dyes among premenopausal dyers alters hormonal levels. Objectives: We aimed at determining the probable effects of occupational exposure to Vat dyes on reproductive

hormones of female textile dyers in the follicular and luteal phases while relating this to age categories and duration of exposure. Methods: Thirty-three premenopausal Vat textile dyers at “Itoku”, Abeokuta, Nigeria, among a population of about 80 female dyers were age and sex-matched with 55 non-exposed (control) female participants. Using semi-structured questionnaires, socio-demographic, occupational details and the LMP of participants were obtained. Serum samples were collected in follicular and luteal phases and assayed for female sex hormones using Enzyme Immunoassay. Mann-Whitney U and Z-statistic were used for comparison of the two groups. P-value < 0.05 was considered to be significant. Results: In the follicular phase, the result showed a lower mean FSH ranking (in age category ≤20 years) and higher ($p<0.05$) Estradiol ranking (in age category 31-40 years) in the exposed than the unexposed. Mean ranks of Progesterone and Estradiol in the luteal phase (age category 31-40 years) were higher ($p<0.05$) in the exposed, while Estradiol (age category ≥41years) ranked lower ($p<0.05$). Prolactin demonstrated a significant inverse relationship with the duration of exposure. Conclusion: Occupational exposure to Vat dye among female dyers in Abeokuta is associated with some sex hormone disruption which appears to be age and duration of exposure-related.
Lien vers l'article

Exposure to Endocrine-Disrupting Chemicals and Congenital Heart Diseases: The Pooled Results Based on the Current Evidence.
Dai J, Wang G, Wu C, Pan Z, Li H, Shen L, et al. *Pediatr Cardiol*. 2024 2024 Apr 11.
The relationships between maternal exposure to endocrine-disrupting chemicals (EDCs) and congenital heart diseases (CHD) are not elucidated yet. The exposure levels of EDCs are generally estimated based on self-reported questionnaires or occupational exposure evaluations in the literature. Therefore, a study based on epidemiological data from human biospecimens is required to provide stronger evidence between maternal exposure to EDC and CHD. Embase, Pubmed, Scopus, and the Cochrane Library databases were searched for related research which provided risk estimates regarding the relationships between maternal EDC exposure and CHD in human offspring. Baseline characteristics and outcomes of CHD were extracted from each included study. Odds ratios (ORs) with 95% confidence intervals (CIs) were pooled to calculate the overall estimates of CHD. Subgroup and meta-regression analyses were performed to identify the sources of heterogeneity. Bootstrapping techniques were used in analyses where several studies originated from a similar population. A total of seventeen studies were involved in the meta-analyses. Maternal EDC exposure was significantly related to CHD in offspring (OR 2.15; 95%CI 1.64 to 2.83). EDC exposure was significantly associated with septal defects (OR 2.34; 95%CI 1.77 to 3.10), conotruncal defects (OR 2.54; 95%CI 1.89 to 3.43), right ventricular outflow tract obstruction (OR 2.65; 95%CI 1.73 to 4.07), left ventricular outflow tract obstruction (OR 3.58; 95%CI 2.67 to 4.79), anomalous pulmonary venous return (OR 2.31; 95%CI 1.34 to 4.00), and other heart defects (OR 2.49; 95%CI 1.75 to 3.54). In addition, maternal exposure to heavy metals, which included lead (OR 2.19; 95%CI 1.29 to 3.71), cadmium (OR 1.81; 95%CI 1.28 to 2.56), mercury (OR 2.23; 95%CI 1.13 to 4.44), and manganese (OR 2.65; 95%CI 1.48 to 4.74), increased risks for CHD significantly. In conclusion, based on the latest evidence, maternal EDC exposure may increase CHD risks in human offspring, especially in heavy metal exposure conditions.
Lien vers l'article

Exposition professionnelle des coiffeuses au résorcinol et fonction thyroïdienne,
PONS R., A. RADAUCEANU, A. ERB, B. ADET, F. DENIS, M.-I. NIOULE, M. DZIURLA and V. MARTIN, *Archives des Maladies Professionnelles et de l'Environnement* 85, no. 2 (2024/05/01/ 2024): 102598,

La France comptabilise environ 70 000 salons de coiffure soit plus de 150 000 professionnels de la coiffure, dont plus de 85 % sont des femmes. Du fait de leur activité professionnelle, celles-ci sont exposées très régulièrement à des perturbateurs endocriniens (PE). Parmi eux, le résorcinol est utilisé dans de nombreuses colorations capillaires et est capable de perturber le fonctionnement de la thyroïde et potentiellement d'entraîner des effets néfastes sur la santé. Cependant, aucune étude épidémiologique n'a été conduite en France à ce jour sur l'exposition professionnelle des coiffeuses au résorcinol et les effets sur la thyroïde. En partenariat avec les services de prévention et de santé au travail (SPST), l'Institut national de recherche et de sécurité (INRS) a initié une étude multidisciplinaire avec pour objectifs : (1) d'évaluer l'exposition professionnelle des coiffeuses au résorcinol, principalement à l'aide de la biométrologie, (2) d'analyser la relation entre cette exposition et différents paramètres de la fonction thyroïdienne mesurés dans le sang. L'exposition professionnelle à d'autres PE sera également prise en compte. Au total, 300 coiffeuses et 150 salariées non exposées professionnellement aux PE, âgées de 18 à 45 ans, seront recrutées par plusieurs SPST de différentes régions de France métropolitaines. Les expositions professionnelles des coiffeuses seront évaluées par questionnaires remplis quotidiennement au cours d'une semaine de travail et par la mesure de certains perturbateurs endocriniens (résorcinol, parabènes et éthylhexyl méthoxycinnamate) dans des échantillons d'urine recueillis à plusieurs reprises au cours d'une même semaine de travail, en début et fin de poste. La fonction thyroïdienne sera évaluée par la mesure de différents paramètres dans le sérum (hormones thyroïdiennes, TSH ou encore anticorps antithyroïdiens), dans une unique prise de sang. Les caractéristiques du salon de coiffure seront également recueillies et un inventaire complet des produits capillaires permettra la constitution d'une base de données compilant les informations sur la toxicité et le potentiel perturbateur endocrinien des substances présentes dans ces produits. Cette étude permettra d'apporter les premières données françaises sur l'effet de l'exposition des coiffeuses au résorcinol et les effets sur la fonction thyroïdienne. Ces données pourront ainsi servir à renforcer les actions de prévention des risques liés aux perturbateurs endocriniens dans cette population.
https://doi.org/10.1016/j.admp.2024.102598

HBM4EU E-waste study: Assessing persistent organic pollutants in blood, silicone wristbands, and settled dust among E-waste recycling workers in Europe,
CSERESZNYE A., E. M. HARDY, Y. A. BAMAI, P. CLEYS, G. POMA, G. MALARVANNAN, P. T. J. SCHEEPERS, S. VIEGAS, C. MARTINS, S. P. PORRAS, T. SANTONEN, L. GODDERIS, J. VERDONCK, K. POELS, M. J. SILVA, H. LOURO, I. MARTINSONE, L. AKULOVA, M. VAN DAEL, A. VAN NIEUWENHUYSE, S. MAHIOUT, R. C. DUCA and A. COVACI, *Environmental Research* 250 (Jun 2024),
E-waste recycling is an increasingly important activity that contributes to reducing the burden of end-of-life electronic and electrical apparatus and allows for the EU's transition to a circular economy. This study investigated the exposure levels of selected persistent organic pollutants (POPs) in workers from e-waste recycling facilities across Europe. The concentrations of seven polychlorinated biphenyls (PCBs) and eight polybrominated diphenyl ethers (PBDEs) congeners were measured by GC-MS. Workers were categorized into five groups based on the type of ewaste handled and two control groups. Generalized linear models were used to assess the determinants of exposure levels among workers. POPs levels were also assessed in dust and silicone wristbands (SWB) and compared with serum. Four PCB congeners (CB 118, 138, 153, and 180) were frequently detected in serum regardless of worker's category. With the exception of CB 118, all tested PCBs were significantly higher in workers compared to the control group. Controls working in the same company as occupationally exposed (Within control group), also displayed higher levels of serum CB 180 than non-industrial controls with no known exposures to these chemicals (Outwith controls) ($p < 0.05$). BDE 209 was the most prevalent POP in settled dust (16 mu g/g) and SWB (220 ng/ WB). Spearman correlation revealed moderate to strong positive correlations between SWB and dust. Increased age and the number of years smoked cigarettes were key determinants for workers

exposure. Estimated daily intake through dust ingestion revealed that sigma PCB was higher for both the 50th (0.03 ng/kg bw/day) and 95th (0.09 ng/kg bw/day) percentile exposure scenarios compared to values reported for the general population. This study is one of the first to address the occupational exposure to PCBs and PBDEs in Europe among e-waste workers through biomonitoring combined with analysis of settled dust and SWB. Our findings suggest that ewaste workers may face elevated PCB exposure and that appropriate exposure assessments are needed to establish effective mitigation strategies. https://doi.org/10.1016/j.envres.2024.118537

Prévention du risque chimique dans les salons de coiffure,
LEVERY G., *Archives des Maladies Professionnelles et de l'Environnement* 85, no. 2 (2024/05/01/ 2024): 102572,
Résumé Initialement, un groupe de travail sur les salons de coiffure a été mis en place en collaboration entre la CARSAT, la DREETS et l'APST37 dans le cadre du plan régional santé au travail. L'APST37 était de plus en plus sollicitée par les coiffeurs suite aux visites et/ou aux courriers de l'inspection du travail, leur demandant un état des lieux des actions de prévention à développer au sein de leurs salons. Il leur était également exigé la réalisation d'une évaluation du risque chimique dans l'objectif de mettre en œuvre des moyens de prévention adaptés. Cependant, la réglementation cosmétique étant très différente de celle des produits chimiques (REACH), il est difficile d'accéder aux informations nécessaires (exemple Fiches de Données Sécurité) pour permettre l'évaluation du risque chimique des produits. De ce fait, il a été proposé d'ouvrir un groupe de travail spécifique pour ce secteur afin de réfléchir à la problématique et de construire un accompagnement adapté. Ce groupe de travail a permis la réalisation de plusieurs rencontres avec les professionnels de ce secteur sur les années 2018 et 2019. L'objectif était de sensibiliser un maximum de professionnels sur les risques liés à cette profession (TMS, risques chimiques) et de permettre la création de différents outils de communication. L'outil Excel COLIBRISK a servi de base de saisie et de données. Des plaquettes et un poster à destination des salons de coiffure ont ainsi été créés sur la base de 1231 substances identifiées parmi 44 marques différentes contenues dans des produits de coiffure répertoriés sur le terrain auprès de salons de coiffure de l'Indre-et-Loire. Une liste des substances dangereuses (perturbateurs endocriniens, CMR, sensibilisants cutanés et respiratoires) à éviter lors de la sélection des produits est présente dans ces supports ainsi que des mesures de prévention adaptées à ce secteur d'activité.
https://doi.org/10.1016/j.admp.2024.102572

PRICABASE : un outil pour approfondir le risque chimique dans l'aéronautique,
ARGILES G., I. HOLECKOVA and V. ESTIENNY-BOUSQUET, *Archives des Maladies Professionnelles et de l'Environnement* 85, no. 2 (2024/05/01/ 2024): 102205,
Résumé Les risques liés aux agents chimiques CMR (cancérogènes, mutagènes et toxiques pour la reproduction) et PE (perturbateurs endocriniens) constituent un enjeu majeur pour la santé des travailleurs du secteur de la sous-traitance aéronautique et spatiale. Les entreprises de ce secteur, nombreuses en Occitanie, ont des difficultés à repérer sur leur lieu de travail ces substances préoccupantes et à mettre en place des actions de substitution ou, à défaut, de réduction ou de maîtrise des risques. Depuis 2017, le PRST (plan régional santé travail) Occitanie se mobilise sur ce sujet au sein du groupe de travail PRICA (prévention du risque chimique dans l'aéronautique). Co-piloté par le service de prévention et de santé au travail toulousain Prevaly et la CARSAT Midi-Pyrénées, ce partenariat inclus la DREETS Occitanie ainsi que 6 autres services de prévention et de santé au travail interentreprises de la région (APREVYA, CSTG32, PRESTAL, SMTI82, SSTMC, SPSTT), 1 association pluridisciplinaire de santé au travail (ASTI) et 3 services de prévention autonomes (AIRBUS, Air France et ERAMET). Le groupe de travail PRICA a développé à l'échelle de la région un outil, appelé la PRICABASE, permettant, d'une part, d'approfondir les résultats des évaluations du

risque chimique conduites par les entreprises et, d'autre part, de les restituer de manière synthétique au médecin du travail, à son équipe pluridisciplinaire ainsi qu'à l'employeur. Concrètement, l'utilisation de la PRICABASE suit 3 étapes : la collecte, l'analyse et la restitution des données. Le service de prévention récupère d'abord l'évaluation du risque chimique de l'entreprise. La PRICABASE est capable d'analyser les évaluations des risques provenant de plusieurs outils d'évaluation. La PRICABASE identifie ensuite la totalité des substances CMR et PE contenues dans les produits que ces dernières soient classées par la classification harmonisée du règlement CLP ou auto-classées par les fournisseurs. La PRICABASE édite enfin un contenu servant de base à la réalisation d'un rapport visuel et pédagogique qui détaille les utilisations des substances préoccupantes pour chaque métier de l'aéronautique présent dans l'entreprise. Le médecin du travail peut ainsi adapter son suivi individuel de l'état de santé et l'entreprise peut plus facilement prioriser ses actions de prévention. À terme, l'outil permettra d'identifier les utilisations des substances CMR et PE dans les métiers de l'aéronautique des entreprises d'Occitanie et permettra de prioriser les prochains travaux du groupe PRICA. https://doi.org/10.1016/j.admp.2024.102205

Santé au travail et Système national des données de santé,
CHAMOT S., C. MANAOUIL, S. FANTONI, P. FRIMAT, A. AL-SALAMEH, R. DESAILLOUD, V. BONNETERRE, A. CHATELAIN and T. BALCAEN, *Archives des Maladies Professionnelles et de l'Environnement* 85, no. 2 (2024/05/01/ 2024): 102271,
Le Système national de données de santé (SNDS) repose sur l'enregistrement et la mise à disposition des données sur les prestations en nature (soins, médicaments, transports…) et espèce (indemnité journalière, rente, capital…) de l'ensemble des régimes d'assurance maladie. Il intègre des informations de santé, des données sur l'activité des établissements hospitaliers, ainsi que sur les causes de décès. L'intégration de données sur le handicap issu des différentes maisons départementales des personnes handicapées est prévue très prochainement. À terme, il est également prévu que des données issues des dossiers médicaux en santé (DMST) au travail soient intégrées. Les modalités d'accès aux données du SNDS s'élargissent et deviennent plus flexibles à mesure que le système se développe, avec encore très récemment l'adoption des méthodologies de référence MR-007 et MR-008 par la Commission nationale de l'informatique et des libertés (CNIL). Ainsi, les centres régionaux de pathologies professionnelles et environnementales (CRPPE) peuvent maintenant bénéficier d'un accès permanent et complet au SNDS. De plus les services de prévention et de santé au travail (SPST) ont la possibilité d'utiliser le numéro d'inscription au répertoire national d'identification des personnes physiques (NIR) comme identifiant de santé des personnes pour la prise en charge des salariés suivis. Dès lors, l'occasion de réaliser des études épidémiologiques à grande échelle s'ouvre pour l'ensemble des acteurs de la santé au travail, sans avoir à attendre l'intégration d'informations du DMST dans le SNDS, dont la nature reste encore à déterminer. Les données recueillies par les SPST concernant les expositions professionnelles sont une mine d'or d'informations pour étudier des thématiques aussi diverses que la grossesse et la périnatalité, les accidents du travail, l'impact de nouvelles technologiques en santé sur le maintien en emploi. Le croisement avec des outils spécialisés comme TOXILIST pourrait permettre d'étudier des problématiques très spécifiques comme celle de l'impact de l'exposition à des perturbateurs endocriniens potentiels sur des populations humaines, avec là encore des retombées majeures en matière de santé publique. Mais ces projets se confrontent encore à des difficultés : hétérogénéité dans la qualité des informations saisies dans le DMST, manque d'interopérabilité des systèmes informatiques, périmètre restreint des données du SNDS, manque d'implication des employeurs dans la traçabilité des expositions professionnelles. Ces freins ne doivent pas empêcher les acteurs de la santé au travail de se saisir de cet outil. Nous présenterons donc les modalités permettant d'apparier les données des SPST au SNDS sur projet. https://doi.org/10.1016/j.admp.2024.102271

Epidémiologie

17-OR: ADA Presidents' Select Abstract: Oral Bisphenol A Administration Decreased Peripheral Insulin Sensitivity in Healthy Adults,
SEAL A., S. K. MALIN, A. SCHAFFNER, M. R. HUBBARD, S. K. KEADLE, H. BRUNNER-GAYDOS, A. A. ORTIZ, J. E. NAKAMURA, C. MCMAHON, R. BARNETT, A. H. KELLEHER, K. A. BENNION, S. PHELAN and T. HAGOBIAN, *Diabetes* 73, no. Supplement_1 (2024),
Introduction: Bisphenol A (BPA) is a synthetic chemical widely used in consumer goods and is linked to Type 2 diabetes progression in observational studies. No experimental studies have examined whether BPA promotes reductions in peripheral insulin sensitivity. Objective: To determine the effects of oral BPA administration on peripheral insulin sensitivity.Methods: Forty non-habitually active, healthy adults (22 F, 18 M; 21.3 ± 2.5 yr; 22.1 ± 2.3 kg/m2; 85% Non-Hispanic White) completed a 2-day baseline energy balance diet low in bisphenols during which urine, blood, and peripheral insulin sensitivity (i.e., glucose infusion rate/steady-state plasma insulin) via 120 min euglycemic hyperinsulinemic clamp technique (40 mU/m2/min; 90 mg/dL) were assessed. Participants were then randomly assigned, in a double-blinded fashion, to a 4-day energy balance diet plus oral BPA administration at 50 µg/kg body weight (BPA-50) or 4-day energy balance diet plus oral placebo (PL) administration. Outcomes were reassessed using a repeated measures ANOVA adjusting for baseline sex, BMI, physical activity, and ethnicity.Results: From baseline to 4-days, body weight was not significantly (P>0.05) different between PL (mean ± SEM; 66.7 ± 2.5, 66.2 ± 2.5 kg) and BPA-50 (66.7 ± 2.5, 66.7± 2.5 kg). From baseline to 4-days, fasting blood glucose was not significantly (P > 0.05) different between PL (95 ± 2, 88 ± 2 mg/dL) and BPA-50 (92 ± 2, 92 ± 2 mg/dL). Compared to PL urine BPA was significantly higher (P<0.05) following BPA-50. From baseline to 4-days, peripheral insulin sensitivity significantly (P=0.01) decreased in BPA-50 (0.11 ± 0.01, 0.10 ± 0.01 mg/kg/min/uU/ml) and remained stable in PL (0.09 ± 0.01, 0.10 ± 0.01 mg/kg/min/uU/ml).Conclusion: BPA administration decreased peripheral insulin sensitivity after four days. These data provide the first experimental evidence that BPA administration may increase Type 2 diabetes risk. Supported by American Diabetes Association grant #1-19-ICTS-044.A. Seal: None. S.K. Malin: None. A. Schaffner: None. M.R. Hubbard: None. S.K. Keadle: None. H. Brunner-Gaydos: None. A.A. Ortiz: None. J.E. Nakamura: None. C. McMahon: None. R. Barnett: None. A.H. Kelleher: None. K.A. Bennion: None. S. Phelan: Research Support; Weight Watchers International. T. Hagobian: None.American Diabetes Association (1-19-ICTS-044) https://doi.org/10.2337/db24-17-OR

Adverse impact of phthalate and polycyclic aromatic hydrocarbon mixtures on birth outcomes: A metabolome Exposome-Wide association study,
FANG Y., W. YIN, C. HE, Q. SHEN, Y. XU, C. LIU, Y. ZHOU, G. LIU, Y. ZHAO, H. ZHANG and K. ZHAO, *Environ Pollut* 357 (Jun 28 2024): 124460,
It has been well-investigating that individual phthalates (PAEs) or polycyclic aromatic hydrocarbons (PAHs) affect public health. However, there is still a gap that the mixture of PAEs and PAHs impacts birth outcomes. Through innovative methods for mixtures in epidemiology, we used a metabolome Exposome-Wide Association Study (mExWAS) to evaluate and explain the association between exposure to PAEs and PAHs mixtures and birth outcomes. Exposure to a higher level of PAEs and PAHs mixture was associated with lower birth weight (maximum cumulative effect: 143.5 g) rather than gestational age. Mono(2-ethlyhexyl) phthalate (MEHP) (posterior inclusion probability, PIP = 0.51), 9-hydroxyphenanthrene (9-OHPHE) (PIP = 0.53), and 1-hydroxypyrene (1-OHPYR) (PIP = 0.28) were identified as the most important compounds in the mixture. In mExWAS, we successfully annotated four overlapping metabolites associated with both MEHP/9-OHPHE/1-OHPYR and birth weight, including arginine, stearamide, Arg-Gln, and valine. Moreover, several

lipid-related metabolism pathways, including fatty acid biosynthesis and degradation, alpha-linolenic acid, and linoleic acid metabolism, were disturbed. In summary, these findings may provide new insights into the underlying mechanisms by which PAE and PAHs affect fetal growth.
https://doi.org/10.1016/j.envpol.2024.124460

The association between endocrine disrupting chemicals and nonalcoholic fatty liver disease: A systematic review and meta-analysis,
PAN K., J. XU, Y. Z. XU, C. X. WANG and J. YU, *Pharmacological Research* 205 (Jul 2024),
Nonalcoholic fatty liver disease (NAFLD) is one of the leading causes of chronic liver disease worldwide. Epidemiological studies have reported that exposure of the population to environmental endocrine-disrupting chemicals (EDCs) is associated with NAFLD. However, EDCs are of different types, and there are inconsistencies in the relevant evidence and descriptions, which have not been systematically summarized so far. Therefore, this study aimed to determine the association between population exposure to EDCs and NAFLD. Three databases, including PubMed, Web of science, and Embase were searched, and 27 articles were included in this study. Methodological quality, heterogeneity, and publication bias of the included studies were assessed using the Newcastle-Ottawa scale, I2 statistics, Begg's test, and Egger's test. The estimated effect sizes of the included studies were pooled and evaluated using the random-effects model (I-2 > 50 %) and the fixed-effects model (I-2 < 50 %). The pooled-estimate effect sizes showed that population exposure to Phthalates (PAEs) (OR = 1.18, 95 % CI:1.03-1.34), cadmium (Cd) (OR = 1.37, 95 % CI:1.09-1.72), and bisphenol A (OR = 1.43, 95 % CI:1.24-1.65) were positively correlated with the risk of NAFLD. Exposure to mercury (OR =1.46, 95 % CI:1.17-1.84) and Cd increased the risk of "elevated alanine aminotransferase". On the contrary, no significant association was identified between perfluoroalkyl substances (OR =0.99, 95 % CI:0.93-1.06) and NAFLD. However, female exposure to perfluorooctanoic acid (OR =1.82, 95 % CI:1.01-3.26) led to a higher risk of NAFLD than male exposure. In conclusion, this study revealed that EDCs were risk factors for NAFLD. Nonetheless, the sensitivity analysis results of some of the meta-analyses were not stable and demonstrated high heterogeneity. The evidence for these associations is limited, and more large-scale population-based studies are required to confirm these findings.
https://doi.org/10.1016/j.phrs.2024.107251

Association between endocrine-disrupting chemical mixtures and non-alcoholic fatty liver disease with metabolic syndrome as a mediator among adults: A population-based study in Korea,
PARK B., B. KIM, C. H. KIM, H. J. OH and B. PARK, *Ecotoxicology and Environmental Safety* 276 (May 2024),
Endocrine -disrupting chemicals (EDCs) may play a role in non-alcoholic fatty liver disease (NAFLD); however, studies on the combined effects of EDC mixtures on NAFLD development are limited. Here, we explored the association between exposure to EDC mixtures and NAFLD and investigated the potential mediating role of metabolic syndrome (MetS). We included participants from the Korean National Environmental Health Survey Cycle 4 (2018 - 2020) and quantified the urinary concentrations of various EDCs - eight phthalate metabolites, three phenols, one antibacterial compound, four parabens, four polycyclic aromatic hydrocarbons, and one pyrethroid pesticide metabolite - as well as serum concentrations of five perfluorinated compounds (PFCs). NAFLD was defined as a hepatic steatosis index (HSI) >= 36 or a fatty liver index (FLI) >= 60. Weighted quantile sum (WQS) regression was employed to evaluate the associations between EDC mixtures and the risk of MetS or NAFLD. Causal mediation analysis was conducted to explore the potential mediating effect of MetS on the association between mixtures of EDCs and NAFLD risk. All estimates were adjusted for age, sex, educational level, physical activity, smoking status, involuntary smoking, and drinking habits. A total of 2942 adults were included in the analysis. Moderate -to -high positive correlations were identified between phthalate metabolites and PFCs. Higher WQS scores were

associated with an elevated risk of MetS and NAFLD. The sex -stratified WQS regression model showed that the interactions between the WQS index and sex were significant for MetS and NAFLD. According to the causal mediation analysis, both the direct and indirect effects of EDC mixtures on NAFLD, with MetS as a mediator, were significant in females. Collectively, these findings highlight the need for interventions that could address both EDC mixture exposure and metabolic status to effectively reduce the risks associated with NAFLD and its related complications. https://doi.org/10.1016/j.ecoenv.2024.116310

The association between heavy metal exposure and obesity: A systematic review and meta-analysis,
ZANGIABADIAN M., A. G. JOLFAYI, S. A. NEJADGHADERI, L. AMIRKHOSRAVI and M. SANJARI, *J Diabetes Metab Disord* 23, no. 1 (Jun 2024): 11-26,
BACKGROUND: Obesity and metabolic syndrome are global health concerns associated with development of different types of diseases and serious health threats in the long term. Their metabolic imbalance can be attributable to inherited and environmental factors. As a considerable environmental agent, heavy metals exposure can predispose individuals to diseases like obesity. This systematic review and meta-analysis aimed to evaluate the association between heavy metals exposure and the risk of obesity. METHODS: PubMed/MEDLINE, EMBASE and Web of Science were systematically searched until December 17, 2022. Only observational studies that evaluated heavy metals exposure and obesity were included. Studies were excluded if they assessed maternal or prenatal exposure, the mixture of heavy metals and other chemicals, reported the association with overweight or other diseases, and undesirable study designs. The Joanna Briggs Institute checklist was used for quality assessment. The pooled adjusted odds ratio (aOR) and the pooled standardized mean difference (SMD) with their 95% confidence intervals (CIs) were calculated, respectively. The publication bias was evaluated using Egger's and Begg's tests. RESULTS: Twenty studies (n = 127755), four case-control and sixteen analytical cross-sectional studies, were included. Lead exposure was significantly associated with a lower risk of obesity (aOR: 0.705, 95% CI: 0.498-0.997), while mercury (aOR: 1.458, 95% CI: 1.048-2.031) and barium (aOR: 1.439, 95% CI: 1.142-1.813) exposure increased the risk of obesity. No significant publication bias was found and the studies had a low risk of bias. CONCLUSION: Overall, lead exposure reduced obesity risk, while mercury and barium exposure raised it. Further large-scale observational studies are recommended to determine the roles of heavy metals in obesity.Study registration ID: CRD42023394865. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s40200-023-01307-0. https://doi.org/10.1007/s40200-023-01307-0

Association between pesticide exposure and thyroid function: analysis of Chinese and NHANES databases,
XU L., S. YANG, L. WANG, J. QIU, H. MENG, L. ZHANG, W. SUN and A. HE, *Front Public Health* 12 (2024): 1378027,
BACKGROUND: Pesticides are widely used in agricultural activities. Although pesticide use is known to cause damage to the human body, its relationship with thyroid function remains unclear. Therefore, this study aimed to investigate the association between pesticide exposure and thyroid function. METHODS: The Chinese database used included 60 patients with pyrethroid poisoning and 60 participants who underwent health checkups between June 2022 and June 2023. The NHANES database included 1,315 adults enrolled from 2007 to 2012. The assessed pesticide and their metabolites included 2,4-dichlorophenoxyacetic acid (2,4-D), 4-fluoro-3-phenoxybenzoic acid (4F3PB), para-nitrophenol (PN), 3-phenoxybenzoic acid (3P), and trans-dichlorovinyl-dimethylcyclopropane carboxylic acid (TDDC). The evaluated indicators of thyroid function were measured by the blood from the included population. The relationship between pesticide exposure and thyroid function indexes was investigated using linear regression, Bayesian kernel machine

regression (BKMR), restricted cubic spline (RCS), and weighted quantile sum (WQS) models. RESULTS: The Chinese data showed that pesticide exposure was negatively correlated with the thyroid function indicators FT4, TT4, TgAb, and TPOAb (all $p < 0.05$). The BKMR model analysis of the NHANES data showed that the metabolic mixture of multiple pesticides was negatively associated with FT4, TSH, and Tg, similar to the Chinese database findings. Additionally, linear regression analysis demonstrated positive correlations between 2,4-D and FT3 ($p = 0.041$) and 4F3PB and FT4 ($p = 0.003$), whereas negative associations were observed between 4F3PB and Tg ($p = 0.001$), 4F3PB and TgAb ($p = 0.006$), 3P and TgAB ($p = 0.006$), 3P and TPOAb ($p = 0.03$), PN and TSH ($p = 0.003$), PN and TT4 ($p = 0.031$), and TDDC and TPOAb ($p < 0.001$). RCS curves highlighted that most pesticide metabolites were negatively correlated with thyroid function indicators. Finally, WQS model analysis revealed significant differences in the weights of different pesticide metabolites on the thyroid function indexes. CONCLUSION: There is a significant negative correlation between pesticide metabolites and thyroid function indicators, and the influence weights of different pesticide metabolites on thyroid function indicators are significantly different. More research is needed to further validate the association between different pesticide metabolites and thyroid disease. https://doi.org/10.3389/fpubh.2024.1378027

Association of maternal exposure to endocrine disruptor chemicals with cardio-metabolic risk factors in children during childhood: a systematic review and meta-analysis of cohort studies, RAHIMLOU M., M. A. MOUSAVI, H. CHITI, M. PEYDA and S. N. MOUSAVI, *Diabetology & Metabolic Syndrome* 16, no. 1 (Apr 2024),
Background In the present systematic review and meta-analysis, the association of maternal exposure to the endocrine disrupting chemicals (EDCs) with cardio-metabolic risk factors in children during childhood for the first time. Method The PubMed, Scopus, EMBASE, and Web of Science databases were systematically searched, up to Feb 2023. In total 30 cohort studies had our inclusion criteria. A random-effects model was used for the variables that had considerable heterogeneity between studies. The Newcastle-Ottawa Scale (NOS) tool was used to classify the quality score of studies. All statistical analyses were conducted using Stata 14 and P-value < 0.05 considered as a significant level. Results In the meta-analysis, maternal exposure to the EDCs was weakly associated with higher SBP (Fisher_Z: 0.06, CI: 0.04, 0.08), BMI (Fisher_Z: 0.07, CI: 0.06, 0.08), and WC (Fisher_Z: 0.06, CI: 0.03, 0.08) z-scores in children. A significant linear association was found between maternal exposure to the bisphenol-A and pesticides with BMI and WC z-score in children ($p < 0.001$). Subgroup analysis showed significant linear association of BPA and pesticides, in the urine samples of mothers at the first trimester of pregnancy, with BMI and WC z-score in children from 2-8 years ($p < 0.05$). Conclusion Prenatal exposure to the EDCs in the uterine period could increase the risk of obesity in children. Maternal exposure to bisphenol-A and pesticides showed the strongest association with the obesity, especially visceral form, in the next generation. https://doi.org/10.1186/s13098-024-01320-0

Association of metals and bisphenols exposure with lipid profiles and dyslipidemia in Chinese adults: Independent, combined and interactive effects, WEI J., R. LIU, Z. YANG, H. LIU, Y. WANG, J. ZHANG, M. SUN, C. SHEN, J. LIU, P. YU and N. J. TANG, *Sci Total Environ* 946 (Jun 26 2024): 174315,
BACKGROUND: Although studies have assessed the association of metals and bisphenols with lipid metabolism, the observed results have been controversial, and limited knowledge exists about the combined and interactive effects of metals and bisphenols exposure on lipid metabolism. METHODS: Plasma metals and serum bisphenols concentrations were evaluated in 888 participants. Multiple linear regression and logistic regression models were conducted to assess individual associations of 18 metals and 3 bisphenols with 5 lipid profiles and dyslipidemia risk, respectively. The dose-response relationships of targeted contaminants with lipid profiles and dyslipidemia risk

were captured by applying a restriction cubic spline (RCS) function. The bayesian kernel machine regression (BKMR) model was used to assess the overall effects of metals and bisphenols mixture on lipid profiles and dyslipidemia risk. The interactive effects of targeted contaminants on interested outcomes were explored by constructing an interaction model. RESULTS: Single-contaminant analyses revealed that exposure to iron (Fe), nickel (Ni), copper (Cu), arsenic (As), selenium (Se), strontium (Sr), and tin (Sn) was associated with elevated lipid levels. Cobalt (Co) showed a negative association with high density lipoprotein cholesterol (HDL-C). Bisphenol A (BPA) and bisphenol AF (BPAF) were associated with decreased HDL-C levels, with nonlinear associations observed. Vanadium (V), lead (Pb), and silver (Ag) displayed U-shaped dose-response relationships with most lipid profiles. Multi-contaminant analyses indicated positive trends between contaminants mixture and total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), and non-high-density lipoprotein cholesterol (non-HDL-C). The interaction analyses showed that Se-Fe exhibited synergistic effects on LDL-C and non-HDL-C, and Se-Sn showed a synergistic effect on HDL-C. CONCLUSIONS: Our study suggested that exposure to metals and bisphenols was associated with changes in lipid levels, and demonstrated their combined and interactive effects. https://doi.org/10.1016/j.scitotenv.2024.174315

Association of urinary bisphenol A with hyperlipidemia and all-cause mortality: NHANES 2003-2016,
GUO L., P. ZHAO, S. XUE and Z. ZHU, *PLoS One* 19, no. 7 (2024): e0304516,
BACKGROUND: The connection between urinary bisphenol A (BPA) and hyperlipidemia is still unclear, and few studies have evaluated whether urinary BPA affects mortality among individuals with hyperlipidemia. Therefore, we aimed to investigate the link between urinary BPA and hyperlipidemia and assess the impact of urinary BPA on mortality risk in subjects with hyperlipidemia. METHODS: We analyzed data of the National Health and Nutrition Examination Survey from 2003 to 2016. Multivariable logistic analysis was performed to examine the relationship between urinary BPA and hyperlipidemia. Cox regression analysis was carried out to investigate the relationship between urinary BPA and all-cause mortality in subjects with hyperlipidemia. RESULTS: This study included 8,983 participants, of whom 6,317 (70.3%) were diagnosed with hyperlipidemia. The results showed that urinary BPA was higher in participants with hyperlipidemia group than those without hyperlipidemia (3.87 ± 0.32 vs. 2.98 ± 0.14, P = 0.01). Urinary BPA levels were analyzed in tertiles. Compared with tertile 1 of BPA (reference), the odds ratio (95% confidence interval) of hyperlipidemia related to tertile 3 of BPA was 1.28 (1.11-1.48). The hazard ratio for all-cause death associated with the highest versus lowest tertile of urinary BPA was 1.20 (95% confidence interval: 1.01-1.44; P = 0.04) among participants with hyperlipidemia. CONCLUSIONS: The study indicated a positive relationship between urinary BPA and the risk of hyperlipidemia. Urinary BPA was associated with a significantly higher risk of all-cause mortality in adults with hyperlipidemia. https://doi.org/10.1371/journal.pone.0304516

Associations between paediatric obesity, chemical mixtures and environmental factors, in a national cross-sectional study of Canadian children,
DUGANDZIC R., N. KONSTANTELOS, Y. YU, E. LAVIGNE, S. SRUGO, J. J. LANG, K. LARSEN, T. POLLOCK, P. VILLENEUVE, E. M. THOMSON, M. MACPHERSON, R. DALES and S. CAKMAK, *Pediatr Obes* (Jun 14 2024): e13117,
BACKGROUND: Whilst single chemical exposures are suspected to be obesogenic, the combined role of chemical mixtures in paediatric obesity is not well understood. OBJECTIVES: We aimed to evaluate the potential associations between chemical mixtures and obesity in a population-based sample of Canadian children. METHODS: We ascertained biomonitoring and health data for children aged 3-11 from the cross-sectional Canadian Health Measures Survey from 2007 to 2019. Several chemicals of interest were measured in blood or urine and paediatric obesity was defined

based on measured anthropometrics. Using quantile-based G computational analysis, we quantified the effects of three chemical mixtures selected a priori. Models were adjusted for sociodemographic and environmental factors identified through a directed acyclic graph. Results are presented through adjusted relative risks (RR) with 95% confidence intervals (95% CI). RESULTS: We included 9147 children. Of these, 24.1% were overweight or obese. Exposure to the mixture of bisphenol A, acrylamide, glycidamide, metals, parabens and arsenic increased the risk of childhood overweight or obesity by 45% (95% CI 1.09, 1.93), obesity by 109% (95% CI 1.27, 3.42) and central obesity by 82% (95% CI 1.30, 2.56). CONCLUSIONS: Our findings support the role of early childhood chemical exposures in paediatric obesity and the potential combined effects of chemicals. https://doi.org/10.1111/ijpo.13117

Associations between paediatric obesity, chemical mixtures and environmental factors, in a national cross-sectional study of Canadian children,
DUGANDZIC R., N. KONSTANTELOS, Y. M. YU, E. LAVIGNE, S. SRUGO, J. J. LANG, K. LARSEN, T. POLLOCK, P. VILLENEUVE, E. M. THOMSON, M. MACPHERSON, R. DALES and S. CAKMAK, *Pediatric Obesity* (2024 Jun 2024),
BackgroundWhilst single chemical exposures are suspected to be obesogenic, the combined role of chemical mixtures in paediatric obesity is not well understood.ObjectivesWe aimed to evaluate the potential associations between chemical mixtures and obesity in a population-based sample of Canadian children.MethodsWe ascertained biomonitoring and health data for children aged 3-11 from the cross-sectional Canadian Health Measures Survey from 2007 to 2019. Several chemicals of interest were measured in blood or urine and paediatric obesity was defined based on measured anthropometrics. Using quantile-based G computational analysis, we quantified the effects of three chemical mixtures selected a priori. Models were adjusted for sociodemographic and environmental factors identified through a directed acyclic graph. Results are presented through adjusted relative risks (RR) with 95% confidence intervals (95% CI).ResultsWe included 9147 children. Of these, 24.1% were overweight or obese. Exposure to the mixture of bisphenol A, acrylamide, glycidamide, metals, parabens and arsenic increased the risk of childhood overweight or obesity by 45% (95% CI 1.09, 1.93), obesity by 109% (95% CI 1.27, 3.42) and central obesity by 82% (95% CI 1.30, 2.56).ConclusionsOur findings support the role of early childhood chemical exposures in paediatric obesity and the potential combined effects of chemicals. https://doi.org/10.1111/ijpo.13117

Associations between synthetic phenols, phthalates, and placental growth/function: a longitudinal cohort with exposure assessment in early pregnancy,
JOVANOVIC N., V. MUSTIELES, M. ALTHUSER, S. LYON-CAEN, N. ALFAIDY, C. THOMSEN, A. K. SAKHI, A. SABAREDZOVIC, S. BAYAT, A. COUTURIER-TARRADE, R. SLAMA and C. PHILIPPAT, *Human Reproduction Open* 2024, no. 2 (Mar 2024),
STUDY QUESTION Is exposure to environmental chemicals associated with modifications of placental morphology and function?SUMMARY ANSWER Phthalates, a class of ubiquitous chemicals, showed an association with altered placental weight, placental vascular resistance (PVR), and placental efficiency. https://doi.org/10.1093/hropen/hoae018

Associations between urinary hydroxylated polycyclic aromatic hydrocarbon biomarker concentrations and measures of timing of delivery and infant size at birth,
CATHEY A. L., J. L. EATON, D. J. WATKINS, Z. Y. ROSARIO PABÓN, C. M. VÉLEZ VEGA, A. N. ALSHAWABKEH, J. F. CORDERO and J. D. MEEKER, *Environ Int* 190 (Jun 22 2024): 108848,
Preterm birth is a leading cause of neonatal mortality and presents significant public health concerns. Environmental chemical exposures during pregnancy may be partially to blame for disrupted delivery timing. Polycyclic aromatic hydrocarbons (PAHs) are products of incomplete

combustion, exposure to which occurs via inhalation of cigarette smoke and automobile exhaust, and ingestion of charred meats. Exposure to PAHs in the US population is widespread, and pregnant women represent a susceptible population to adverse effects of PAHs. We aimed to investigate associations between gestational exposure to PAHs and birth outcomes, including timing of delivery and infant birth size. We utilized data from the PROTECT birth cohort where pregnant women provided spot urine samples at up to three study visits (median 16, 20, and 24 weeks gestation). Urine samples were assayed for eight hydroxylated PAH concentrations. Associations between PAHs and birth outcomes were calculated using linear/logistic regression models, with adjustment for maternal age, education, pre-pregnancy BMI, and daily exposure to environmental tobacco smoke. Models accounted for urine dilution using specific gravity. We also explored effect modification by infant sex. Interquartile range (IQR) increases in all averaged PAH exposures during the second trimester were associated with reduced gestational age at delivery and increased odds of overall PTB, although these associations were not statistically significant ($p > 0.05$). Most PAHs at the second study visit were most strongly associated with earlier delivery and increased odds of overall and spontaneous PTB, with visit 2 2-hydroxynapthalene (2-NAP) being significantly associated with increased odds of overall PTB (OR:1.55; 95 %CI: 1.05,2.29). Some PAHs resulted in earlier timing of delivery among only female fetuses, specifically 2-NAP on overall PTB (female OR:1.52 95 %CI: 1.02,2.27; male OR:0.78, 95 %CI: 0.53,1.15). Future work should more deeply investigate differential physiological impacts of PAH exposure between pregnancies with male and female fetuses, and on varying developmental processes occurring at different points through pregnancy. https://doi.org/10.1016/j.envint.2024.108848

Co-exposure to 55 endocrine-disrupting chemicals linking diminished sperm quality: Mixture effect, and the role of seminal plasma docosapentaenoic acid,
GAO C., N. SUN, J. Y. XIE, J. H. LI, L. TAO, L. J. GUO, L. SHI, X. J. HE, X. T. SHEN, H. WANG, P. YANG, A. COVACI and Y. C. HUANG, *Environment International* 185 (Mar 2024),
Isolated effects of single endocrine-disrupting chemicals (EDCs) on male reproductive health have been studied extensively, but their mixture effect remains unelucidated. Previous research has suggested that consuming diet enriched in omega-3 polyunsaturated fatty acids (PUFA) might be beneficial for reproductive health, whether omega-3 PUFA could moderate the effect of EDCs mixture on semen quality remains to be explored. In this study of 155 male recruited from a reproductive health center in China, we used targeted-exposomics to simultaneously measure 55 EDCs in the urine for exposure burden. Regression analyses were restricted to highly detected EDCs (>= 55%, n = 34), and those with consistently elevated risk were further screened and brought into mixture effect models (Bisphenol A, ethyl paraben, methyl paraben [MeP], benzophenone-1 [BP1], benzophenone-3, mono(3-carboxypropyl) phthalate [MCPP]). Bayesian Kernel Machine Regression (BKMR) and quantile-based g-computation (QGC) models demonstrated that co-exposure to top-ranked EDCs was related to reduced sperm total (beta = -0.18, 95%CI: -0.29 - -0.07, P = 0.002) and progressive motility (beta = -0.27, 95%CI: -0.43 - -0.10, P = 0.002), but not to lower semen volume. BP1, MeP and MCPP were identified as the main effect driver for deteriorated sperm motion parameters using mixture model analyses. Seminal plasma fatty acid profiling showed that high omega-3 PUFA status, notably elevated docosapentaenoic acid (DPA, C22:5n-3) status, moderated the association between MCPP and sperm motion parameters (total motility: beta = 0.26, 95% CI: 0.01 - -0.51, Pinteraction = 0.047; progressive motility: beta = 0.64, 95%CI: 0.23 - 1.05, Pinteraction = 0.003). Coexposure to a range of EDCs is mainly associated with deteriorated sperm quality, but to a lesser extent on sperm quantity, high seminal plasma DPA status might be protective against the effect. Our work emphasizes the importance of exposomic approach to assess chemical exposures and highlighted a new possible intervention target for mitigating the potential adverse effect of EDCs on semen quality. https://doi.org/10.1016/j.envint.2024.108571

Connecting Bisphenol A Exposure to PCOS: Findings from a Case-Control Investigation,
PATEL J., H. CHAUDHARY, S. PANCHAL, B. PAREKH and R. JOSHI, *Reproductive Sciences* (2024 Apr 2024),
Polycystic Ovary Syndrome (PCOS) is a multifaceted condition influenced by genetic, hormonal, and environmental factors. Among environmental factors, Bisphenol A (BPA)-a recognized endocrine disruptor-has been implicated in the development of PCOS. The study aimed to compare BPA levels in women diagnosed with PCOS with those in healthy controls, using the high-performance liquid chromatography (HPLC) technique. The study involved 80 women diagnosed with PCOS and 50 healthy control participants. Demographic and biochemical parameters were recorded, including age, Body Mass Index (BMI), and levels of testosterone, estradiol, Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), Prolactin (PRL), Dehydroepiandrosterone Sulfate (DHEA-S), Thyroid Stimulating Hormone (TSH), and Insulin Resistance as measured by the Homeostatic Model Assessment (HOMA-IR). Furthermore, BPA levels were measured using the HPLC technique. Women with PCOS exhibited significantly higher mean age and BMI compared to healthy controls ($p = 0.01$, $p < 0.0001$, respectively). Additionally, higher levels of testosterone ($p = 0.04$), LH ($p = 0.03$) and BPA ($p < 0.0001$) were observed in women with PCOS. However, estradiol, FSH, PRL, LH/FSH ratio, DHEA-S, and TSH levels were not significantly different between the two groups. HOMA-IR levels were not recorded for the control group. A notable positive relationship emerged between Bisphenol A and luteinizing hormone (LH) levels ($r = 0.23$, $p = 0.03$), also significant negative correlation appeared between Bisphenol A and thyroid-stimulating hormone (TSH) levels. This study found that women with PCOS have elevated BPA levels compared with healthy controls, showing a need for further research on the relationship between BPA exposure and the development of PCOS. https://doi.org/10.1007/s43032-024-01548-1

Early childhood exposures to phthalates in association with attention-deficit/hyperactivity disorder behaviors in middle childhood and adolescence in the ReCHARGE study,
OH J., J. B. SCHWEITZER, J. P. BUCKLEY, S. UPADHYAYA, K. KANNAN, J. B. HERBSTMAN, A. GHASSABIAN, R. J. SCHMIDT, I. HERTZ-PICCIOTTO, D. H. BENNETT and I. PROGRAM COLLABORATORS ENVIRONM, *International Journal of Hygiene and Environmental Health* 259 (Jun 2024),
Background: Early-life exposure to phthalates alters behaviors in animals. However, epidemiological evidence on childhood phthalate exposure and attention-deficit/hyperactivity disorder (ADHD) behaviors is limited. Methods: This study included 243 children from the ReCHARGE (Revisiting Childhood Autism Risks from Genetics and Environment) study, who were previously classified as having autism spectrum disorder (ASD), developmental delay, other early concerns, and typical development in the CHARGE case-control study. Twenty phthalate metabolites were measured in spot urine samples collected from children aged 2-5 years. Parents reported on children's ADHD symptoms at ages 8-18 years using Conners-3 Parent Rating Scale. Covariateadjusted negative binomial generalized linear models were used to investigate associations between individual phthalate metabolite concentrations and raw scores. Weighted quantile sum (WQS) regression with repeated holdout validation was used to examine mixture effects of phthalate metabolites on behavioral scores. Effect modification by child sex was evaluated. Results: Among 12 phthalate metabolites detected in >75% of the samples, higher mono-2-heptyl phthalate (MHPP) was associated with higher scores on Inattentive (8 per doubling = 0.05, 95% confidence interval [CI]: 0.02, 0.08) and Hyperactive/Impulsive scales (8 = 0.04, 95% CI: 0.00, 0.07), especially among children with ASD. Higher mono-carboxy isooctyl phthalate (MCiOP) was associated with higher Hyperactivity/Impulsivity scores (8 = 0.07, 95% CI: -0.01, 0.15), especially among typically developing children. The associations of the molar sum of high molecular weight (HMW) phthalate metabolites and a phthalate metabolite mixture with Hyperactivity/Impulsivity scores were modified by sex, showing more pronounced adverse associations among females. Conclusion:

Exposure to phthalates during early childhood may impact ADHD behaviors in middle childhood and adolescence, particularly among females. Although our findings may not be broadly generalizable due to the diverse diagnostic profiles within our study population, our robust findings on sex-specific associations warrant further investigations. https://doi.org/10.1016/j.ijheh.2024.114377

Environmental Exposure to Persistent Organic Pollutants and Its Association with Endometriosis Risk: Implications in the Epithelial-Mesenchymal Transition Process,
MARTÍN-LEYVA A., F. M. PEINADO, O. OCÓN-HERNÁNDEZ, A. OLIVAS-MARTÍNEZ, A. LUQUE, J. LEÓN, I. LENDÍNEZ, J. CARDONA, A. LARA-RAMOS, N. OLEA, M. F. FERNÁNDEZ and F. ARTACHO-CORDÓN, *International Journal of Molecular Sciences* 25, no. 8 (Apr 2024),
We aimed to explore the relationship of adipose tissue concentrations of some persistent organic pollutants (POPs) with the risk of endometriosis and the endometriotic tissue expression profile of genes related to the endometriosis-related epithelial-mesenchymal transition (EMT) process. This case-control study enrolled 109 women (34 cases and 75 controls) between January 2018 and March 2020. Adipose tissue samples and endometriotic tissues were intraoperatively collected to determine concentrations of nine POPs and the gene expression profiles of 36 EMT-related genes, respectively. Associations of POPs with endometriosis risk were explored with multivariate logistic regression, while the relationship between exposure and gene expression profiles was assessed through Spearman correlation or Mann-Whitney U tests. After adjustment, increased endometriosis risk was associated with p,p'-DDT, PCB-180, and Sigma PCBs. POP exposure was also associated with reduced gene expression levels of the CLDN7 epithelial marker and increased levels of the ITGB2 mesenchymal marker and a variety of EMT promoters (HMGA1, HOXA10, FOXM1, DKK1, CCR1, TNFRSF1B, RRM2, ANG, ANGPT1, and ESR1). Our findings indicate that exposure to POPs may increase the risk of endometriosis and might have a role in the endometriosis-related EMT development, contributing to the disease onset and progression. Further studies are warranted to corroborate these findings. https://doi.org/10.3390/ijms25084420

Evaluating associations of bisphenol and phthalate exposure with time to pregnancy and subfecundity in a New York City pregnancy cohort,
CHARIFSON M., E. SEOK, Y. Y. WANG, S. S. MEHTA-LEE, R. GORDON, M. L. LIU, L. TRASANDE and L. G. KAHN, *Environmental Pollution* 356 (Sep 2024),
It is important to understand the impact of consumer chemical exposure and fecundity, a couple's measure of probability of successful conception, given approximately 15% of couples experience infertility. Prior research has generally found null associations between bisphenol and phthalate exposure and fecundability, measured via time to pregnancy (TTP). However, this research has not been updated with current chemical exposures and have often lacked diversity in their study populations. We evaluated the associations between common bisphenol and phthalate chemical exposure groups and TTP as well as subfecundity (TTP>12 months) in the New York University Children's Health Study, a diverse pregnancy cohort from 2016 onward. Using first-trimester spot-urine samples to measure chemical exposure and self-reported TTP from first-trimester questionnaires, we observed a significant adverse association between total bisphenol exposure and certain phthalate groups on TTP and odds of subfecundity. Furthermore, in a mixtures analysis to explore the joint effects of the chemical groups on the outcomes, we found evidence of a potential interaction between total bisphenol exposure and low-molecular weight phthalates on TTP. Future research should continue to update our knowledge regarding the complex and potentially interacting effects of these chemicals on reproductive health.
https://doi.org/10.1016/j.envpol.2024.124281

Arsenic and type 2 diabetes: Revealing the environmental exposure relationship through effective factors- A systematic review,

ABOLLI S., S. DEHGHANI, R. ATLASI, Z. MALEKI, M. YUNESIAN, O. TABATABAEI-MALAZY, M. SARAEI, M. KHOSRAVIFAR and Z. SOLEIMANI, *Results in Engineering* 22 (Jun 2024),
This systematic review focoused on exploring the link between environmental exposure to arsenic (in air, water, and food pathways) and the occurrence of type 2 diabetes mellitus (T2DM). A comprehensive search was carried out in PubMed, Scopus, Web of Science, and Embase databases without time and location limits. The inclusion criteria were studied, and 121 records were included after full screening. The reviewed studies primarily focused on arsenic levels in water samples, followed by urine, blood, serum, and plasma samples analysis. Air, food, diet, nail, and tear samples were in the next rank. Many studies concentrated on females and occasionally pregnancy. Some explored arsenic's impact in occupational settings, while others investigated age, obesity, body mass index, and genetic effects. A few studies were related to the Strong Heart Study (SHS), additives, vitamin D, growth promoters, and agricultural product ripening. Arsenic can contaminate groundwater sources, particularly in areas with natural deposits of arsenic or due to industrial activities. Arsenic can be present in certain foods, especially rice, seafood, and poultry; it is also possible to be emitted into the atmosphere via industrial processes such as mining, smelting, and coal combustion and cause occupational exposure. Genetic elements could also contribute to the link between arsenic exposure and the development of T2DM. This association has been observed in both occupational settings and populations with high levels of arsenic in their diets. In the field of limitations, there was restricted data available regarding the gender-specific effects of environmental arsenic exposure on the onset of T2DM, as well as the connection between arsenic exposure, age, and T2DM development. However, the exact molecular mechanisms still need to be fully understood for the correlation between arsenic exposure and T2DM.
https://doi.org/10.1016/j.rineng.2024.102054

Exposure to outdoor ambient air toxics and risk of breast cancer: The multiethnic cohort,
HECK J. E., D. HE, S. E. WING, B. RITZ, C. D. CAREY, J. YANG, D. O. STRAM, L. LE MARCHAND, S. L. PARK, I. A. CHENG and A. H. WU, *International Journal of Hygiene and Environmental Health* 259 (Jun 2024),
Background: A growing literature has reported associations between traffic -related air pollution and breast cancer, however there are fewer investigations into specific ambient agents and any putative risk of breast cancer development, particularly studies occurring in populations residing in higher pollution areas such as Los Angeles. Objectives: To estimate breast cancer risks related to ambient air toxics exposure at residential addresses. Methods: We examined the relationships between ambient air toxics and breast cancer risk in the Multiethnic Cohort among 48,665 California female participants followed for cancer from 2003 through 2013. We obtained exposure data on chemicals acting as endocrine disruptors or mammary gland carcinogens from the NationalScale Air Toxics Assessment. Cox proportional hazards models were used to estimate breast cancer risk per one interquartile range (IQR) increase in air toxics exposure lagged by 5 -years. Stratified analyses were conducted by race, ethnicity, and hormone receptor types. Results: Among all women, increased risks of invasive breast cancer were observed with toxicants related to industries [1,1,2,2-tetrachloroethane (hazard ratio [HR] = 4.22, 95% confidence interval [95% CI] 3.18 -5.60), ethylene dichloride (HR = 2.81, 95% CI 2.20 -3.59), and vinyl chloride (HR = 2.27, 95% CI 1.81, 2.85); these 3 agents were correlated (r2 = 0.45 -0.77)]. Agents related to gasoline production or combustion were related to increased breast cancer risk [benzene (HR = 1.32, 95% CI 1.24, 1.41), ethylbenzene (HR = 1.20, 95% CI 1.13 -1.28), toluene (HR = 1.29, 95% CI 1.20 -1.38), naphthalene (HR = 1.11, 95% CI 1.02 -2.22), acrolein (HR = 2.26, 95% CI 1.92, 2.65)]. Higher hazard ratios were observed in African Americans and Whites compared to other racial and ethnic groups (p -heterogeneity <0.05 for traffic -related air toxics, acrolein, and vinyl acetate). Conclusions: Our

findings suggest that specific toxic air pollutants may be associated with increase breast cancer risk. https://doi.org/10.1016/j.ijheh.2024.114362

Exposure to endocrine disrupting chemicals (bisphenols, parabens, and triclosan) and their associations with preterm birth in humans,
KEK T., K. GERSAK and I. VIRANT-KLUN, *Reproductive Toxicology* 125 (Apr 2024),
Preterm birth in humans (PTB), defined as birth prior to 37 weeks of gestation, is one of the most important causes of neonatal morbidity and mortality and is associated with adverse health outcomes later in life. Attributed to many different etiological factors, estimated 15.1 million or 11.1% of births each year are preterm, which is more than 1 per 10 livebirths globally. Environmental pollution is a well-established risk factor that could influence the pathogenesis of PTB. Increasing evidence has shown an association between maternal exposure to endocrine disrupting chemicals (EDCs) and PTB. This scoping review aims to summarize current research on the association between EDC exposure and PTB in humans. Database PubMed was used to identify articles discussing the effect of selected EDCs, namely bisphenol A, bisphenol S, bisphenol F, parabens, and triclosan, found in plastics, cosmetics and other personal care products, on PTB occurrence. Regardless of some inconsistences in the findings across studies, the reviewed studies suggest a potential association between involuntary exposure to reviewed EDCs and the risk of PTB. However, further studies are needed to delineate exact correlations and mechanisms through which EDC exposure causes PTB so that efficient preventative measures could be implemented. Until then, health care providers should inform women about possible EDC exposure thus empowering them to make healthy choices and at the same time decrease the EDC negative effects. https://doi.org/10.1016/j.reprotox.2024.108580

Exposure to environmental pollutants and genetic variants related to oxidative stress and xenobiotic metabolism-Association with prostate cancer,
ALVAREZ-GONZÁLEZ B., A. F. HERNÁNDEZ, A. ZAFRA-GÓMEZ, L. CHICA-REDECILLAS, S. CUENCA-LÓPEZ, F. VÁZQUEZ-ALONSO, L. J. MARTÍNEZ-GONZÁLEZ and M. J. ALVAREZ-CUBERO, *Environmental Toxicology and Pharmacology* 108 (Jun 2024),
This study assessed whether genetic variants coding for certain enzymes involved in xenobiotic detoxification, antioxidant defences and DNA repair, along with exposure to environmental chemicals, were associated with an increased prostate cancer (PCa) risk. The study population consisted of 300 men (150 PCa cases and 150 controls) which underwent prostate biopsy as their serum prostate specific antigen (PSA) levels were greater than 4 ng/ml. Genetic variants in GSTM1, GSTP1, SOD2 , CAT , GPX1 , XRCC1 were determined and data for chemical exposures was obtained through a structured questionnaire and by biomonitoring in a subsample of cases and controls. High serum PSA levels were associated with a greater risk of PCa, while physical exercise appears to exert a protective effect against its development. In addition, elevated urinary levels of certain organic pollutants, such as benzo(a)pyrene (BaP), bisphenol A (BPA), and ethyl-paraben (EPB), were associated with an increased risk of PCa. https://doi.org/10.1016/j.etap.2024.104455

Exposure to organophosphate esters and maternal-child health,
SHAHIN S., E. A. MEDLEY, M. NAIDU, L. TRASANDE and A. GHASSABIAN, *Environmental Research* 252 (Jul 2024),
Organophosphate esters (OPEs) are a class of chemicals now widely used as flame retardants and plasticizers after the phase-out of polybrominated diphenyl ethers (PBDEs). However, OPEs carry their own risk of developmental toxicity, which poses concern for recent birth cohorts as they have become ubiquitous in the environment. In this review, we summarize the literature evaluating the association between OPE exposure and maternal, perinatal, and child health outcomes. We

included original articles investigating associations of OPE exposure with any health outcome on pregnant women, newborns, children, and adolescents. We found 48 articles on this topic. Of these, five addressed maternal health and pregnancy outcomes, 24 evaluated prenatal OPE exposure and child health, 18 evaluated childhood OPE exposure and child/adolescent health, and one article evaluated both prenatal and childhood OPE exposure. These studies suggest that OPE exposure is possibly associated with a wide range of adverse health outcomes, including pregnancy loss, altered gestational duration and smaller birthweight, maternal and neonatal thyroid dysfunction, child metabolic dysregulation and abnormal growth, impaired neurodevelopment, and changes in immune response. Many of the reported outcomes associated with OPE exposure varied by child sex. Findings also varied substantially by OPE metabolite and exposure time. The OPEs most frequently measured, detected, and found to be associated with health outcomes were triphenyl phosphate (TPHP, metabolized to DPHP) and tris(1,3-dichloro-2-propyl) phosphate (TDCIPP, metabolized to BDCIPP). The extensive range of health outcomes associated with OPEs raises concern about their growing use in consumer products; however, these findings should be interpreted considering the limitations of these epidemiological studies, such as possible exposure misclassification, lack of generalizability, insufficient adjustment for covariates, and failure to consider chemical exposures as a mixture. https://doi.org/10.1016/j.envres.2024.118955

Fetal and Infancy Exposure to Phenols, Parabens, and Phthalates and Anthropometric Measurements up to 36 Months, in the Longitudinal SEPAGES Cohort,
OUIDIR M., A. H. CISSÉ, J. BOTTON, S. LYON-CAEN, C. THOMSEN, A. K. SAKHI, A. SABAREDZOVIC, S. BAYAT, R. SLAMA, B. HEUDE and C. PHILIPPAT, *Environmental Health Perspectives* 132, no. 5 (2024): 057002, https://ehp.niehs.nih.gov/doi/abs/10.1289/EHP13644

Gender-specific abdominal fat distribution and insulin resistance associated with organophosphate esters and phthalate metabolites exposure,
SHI X. L., W. Y. WANG, J. F. FENG, X. C. MA, M. T. XU and C. WANG, *Environmental Pollution* 349 (May 2024),
The worldwide prevalence of obesity highlights the potential contribution of endocrine -disrupting chemicals (EDCs). However, common epidemiological measures such as body mass index and waist circumference may misrepresent the intricate obesity risks these chemicals pose across genders. This study delves deeper into abdominal fat by differentiating between subcutaneous and visceral regions by analyzing data from National Health and Nutrition Examination Surveys (NHANES). We particularly investigated the gender -specific associations between organophosphorus flame-retardant metabolites (mOPFRs), phthalates (mPAEs) and accumulated fat indexes from 2536 people. Aiding by Bayesian Kernel Machine Regression (BKMR), we found while co -exposure to mOPFRs and mPAEs was linked to general and abdominal obesity across the entire and gender -specific populations, a gender -specific fat distribution emerged. For women, urinary BDCPP and MBzP were linked to an increased subcutaneous fat index (SFI) [BDCPP OR: 1.12 (95% CI: 1.03 - 1.21), MBzP OR: 1.09 (95% CI: 1.01 - 1.18)], but not to visceral fat index (VFI). These metabolites had a combined linkage with SFI, with BDCPP (weighting 22.0%) and DPHP (weighting 31.0%) being the most influential in Quantile gcomputation model (qgcomp) model. In men, BCEP exposure exclusively associated with the elevated VFI [OR: 1.14 (95% CI: 1.03 - 1.26)], a trend further highlighted in mixture models with BCEP as the predominant association. Intriguingly, only males displayed a marked correlation between these metabolites and insulin resistance in subpopulation. An attempted mediation analysis revealed that elevated C -reactive protein mediated 12.1% of the association between urinary BCEP and insulin resistance, suggesting a potential role of inflammation. In conclusion, the gender -specific fat distribution and insulin resistance that

associated with mOPFRs represented the potential risk of these chemicals to man.
https://doi.org/10.1016/j.envpol.2024.123959

High seminal BPA in IVF patients correlates with lower sperm count and up-regulated miR-21 and miR-130a,
DAVIS O. S., O. L. M. SCANDLAN, R. SABRY, M. GHAFFARZADEH, T. G. HANNAM, A. LAGUNOV and L. A. FAVETTA, *Reprod Toxicol* 128 (Jun 24 2024): 108651,
Bisphenol A (BPA) is a widespread industrial chemical, used as the key monomer of polycarbonate plastics and epoxy resins. BPA has been detected in human seminal fluid and has been correlated with changes in sperm parameters, crucial in determining male fertility. In this study, semen samples were collected from 100 patients aged 29-47 years undergoing fertility assessment between 2021 and 2023 and analyzed according to WHO guidelines. BPA levels in the seminal plasma were then measured through an enzyme-linked immunosorbent assay (ELISA) and compared to sperm quality metrics. The relative mRNA/miRNA expression of key genes associated to male reproduction, including androgen receptor, miR-34c, miR-21, miR-130a, was then quantified and compared between groups with high or low BPA content. Our results revealed that BPA levels were increased with age and were negatively correlated with sperm counts ($p<0.05$). The negative correlation remained significant when patients were age-matched. No other relationships between seminal BPA and motility, morphology or DNA fragmentation levels were observed. qPCR analysis showed that androgen receptor mRNA expression was significantly greater in sperm with high seminal BPA ($p<0.05$). Moreover, we found that the expression of miR-21 and miR-130a was also upregulated in the higher BPA group ($p<0.05$). These results display a relationship between BPA content in the semen and male fertility parameters, and provide insights into the molecular mechanisms through which BPA may be affecting male reproductive capability. Ultimately, this research can potentially drive changes to guidelines and exposure limits for BPA exposure.
https://doi.org/10.1016/j.reprotox.2024.108651

Intrauterine Exposure to Phthalates and Child Growth in the First Year of Life: Results from the BiTwin Cohort,
RIBEIRO C., H. BARROS, M. SEVERO, A. K. SAKHI, C. THOMSEN and E. RAMOS, *Exposure and Health* (2024 Jun 2024),
Phthalates are among the endocrine-disrupting compounds with higher widespread in daily life. Our objective was to assess the associations between maternal exposure to phthalates assessed by urinary phthalate metabolites and growth at birth and in the first year of life. The BiTwin cohort (479 single and 246 multiple pregnancies) was recruited as part of the HEALS project (2017-2019). Evaluations were conducted at birth, 4, 8, and 12 months after childbirth. To mitigate the dependency on twins, we randomly selected one child per family. Birth weight was abstracted from clinical files, and parameters for the first year were based on the child health book. The maternal urine was collected at birth, and phthalate metabolites were determined by liquid chromatography coupled to tandem mass spectrometry. The association between weight growth curves and phthalates was estimated by fixed regression coefficients and 95% confidence intervals calculated through linear mixed effects models. All models include a fixed effect for time and time square and a random intercept and slope by individual. For birth weight, after adjustment, overall, a negative association was found but only statistically significant for mono-n-butyl phthalate metabolite beta = - 0.195 (95% CI - 0.372; - 0.018). In general, the results are similar by sex, but for di(2ethylhexyl) phthalate and cyclohexane-1,2-dicarboxylate, we found associations in the opposite directions. Regarding growth trajectories for the first year of life, overall, no statistically significant associations were found. However, the sum of di(2ethylhexyl) phthalate metabolites presented a positive statistically significant association beta = 0.062 (95%CI 0.002; 0.121) after further adjustment for breastfeeding duration. A positive association was also found for Mono-iso-butyl phthalate in males

(beta = 0.236 (95%CI 0.063; 0.409)). Higher maternal phthalate concentrations tended to be associated with lower birth weight, although they did not reach statistical significance. Regarding the first year of life, di(2ethylhexyl) phthalate presented a positive statistically significant association with growth. https://doi.org/10.1007/s12403-024-00637-5

Maternal exposure to bisphenols, phthalates, perfluoroalkyl acids, and trace elements and their associations with gestational diabetes mellitus in the APrON cohort,
SOOMRO M. H., G. ENGLAND-MASON, A. J. F. REARDON, J. Y. LIU, A. M. MACDONALD, D. W. KINNIBURGH, J. W. MARTIN, D. DEWEY and A. P. S. TEAM, *Reproductive Toxicology* 127 (Aug 2024),
The increasing global prevalence of gestational diabetes mellitus (GDM) has been hypothesized to be associated with maternal exposure to environmental chemicals. Here, among 420 women participating in the Alberta Pregnancy Outcomes and Nutrition (APrON) cohort study, we examined associations between GDM and second trimester blood or urine concentrations of endocrine disrupting chemicals (EDCs): bisphenol-A (BPA), bisphenolS (BPS), twelve phthalate metabolites, eight perfluoroalkyl acids (PFAAs), and eleven trace elements. Fifteen (3.57%) of the women were diagnosed with GDM, and associations between the environmental chemical exposures and GDM diagnosis were examined using multiple logistic and LASSO regression analyses in single- and multi - chemical exposure models, respectively. In single chemical exposure models, BPA and mercury were associated with increased odds of GDM, while a significant inverse association was observed for zinc. DoubleLASSO regression analysis selected mercury (AOR: 1.51, CI: 1.12 -2.02), zinc (AOR: 0.017, CI: 0.0005 -0.56), and perfluoroundecanoic acid (PFUnA), a PFAAs, (AOR: 0.43, CI: 0.19 -0.94) as the best predictors of GDM. The combined data for this Canadian cohort suggest that second trimester blood mercury was a robust predictor of GDM diagnosis, whereas blood zinc and PFUnA were protective factors. Research into mechanisms that underlie the associations between mercury, zinc, PFUnA, and the development of GDM is needed.
https://doi.org/10.1016/j.reprotox.2024.108612

Maternal phthalate exposure and BMI trajectory in children-an 18-year birth cohort follow-up study,
WEN H. J., P. H. SU, C. W. SUN, S. F. TSAI and S. L. WANG, *Journal of Exposure Science and Environmental Epidemiology* (2024 Jun 2024),
BackgroundObesity is a major health concern worldwide. Previous studies have suggested that phthalate plasticizers are obesogens. However, the relationship between early-life phthalate exposure and long-term obesity development remains unknown.ObjectiveWe investigated the association between prenatal phthalate exposure and children's body mass index (BMI) patterns in an 18-year birth cohort follow-up study in Taiwan.MethodsOur analytical lab quantified seven phthalate metabolites in maternal urine during pregnancy using quantitative liquid chromatography-tandem mass spectrometry. In addition, we calculated BMI z scores for participated children at each follow-up, utilized trajectory analysis to describe children's BMI z-score patterns at 2-18 years of age, and adopted generalized estimating equations (GEE) and multivariate logistic regression models to assess the association between prenatal phthalate exposure and BMI z scores in children.ResultsA total of 208 mother-child pairs were included in the analysis. Maternal urinary diethyl phthalate (DEP) metabolites were associated with the increase of BMI z scores in children aged 2-18 years in the GEE model. Doubled maternal urinary ∑mDEHP (3 mono hexyl-metabolites of di-ethyl-hexyl phthalate (DEHP) increased the risk of children being in the stable-high BMI trajectory group until the age of eighteen.Impact statementWe observed that BMI trajectories of children remained stable after the age of 5 years. During each follow-up, a higher frequency of overweight or obese was observed in children, ranging from 15.9% to 35.6% for girls and 15.2-32.0% for boys, respectively. Prenatal phthalate exposure was associated with

increasing BMI z scores in children. Prenatal DEHP exposure was associated with a stable-high BMI trajectory in children up to the age of 18 years. https://doi.org/10.1038/s41370-024-00696-5

Maternal pre-pregnancy BMI influences the associations between bisphenol and phthalate exposures and maternal weight changes and fat accumulation,
IRVINE N., R. C. BELL, F. B. SUBHAN, C. J. FIELD, J. Y. LIU, A. M. MACDONALD, D. W. KINNIBURGH, J. W. MARTIN, D. DEWEY, G. ENGLAND-MASON and A. P. S. TEAM, *Environmental Research* 257 (Sep 2024),
Background: Bisphenols and phthalates are two classes of endocrine-disrupting chemicals (EDCs) thought to influence weight and adiposity. Limited research has investigated their influence on maternal weight changes, and no prior work has examined maternal fat mass. We examined the associations between exposure to these chemicals during pregnancy and multiple maternal weight and fat mass outcomes. Methods: This study included a sample of 318 women enrolled in a Canadian prospective pregnancy cohort. Second trimester urinary concentrations of 2 bisphenols and 12 phthalate metabolites were quantified. Selfreported and measured maternal weights and measured skinfold thicknesses were used to calculate gestational weight gain, 3-months and 3- to 5-years postpartum weight retention, late pregnancy fat mass gain, total postpartum fat mass loss, and late postpartum fat mass retention. Adjusted robust regressions examined associations between chemicals and outcomes in the entire study population and sub-groups stratified by prepregnancy body mass index (BMI). Bayesian kernel machine regression examined chemical mixture effects. Results: Among women with underweight or normal pre-pregnancy BMIs, MBzP was negatively associated with weight retention at 3- to 5-years postpartum (B = -0.04, 95%CI: -0.07, -0.01). Among women with overweight or obese pre-pregnancy BMIs, MEHP and MMP were positively associated with weight retention at 3-months and 3- to 5-years postpartum, respectively (B's = 0.12 to 0.63, 95%CIs: 0.02, 1.07). DEHP metabolites and MCNP were positively associated with late pregnancy fat mass gain and late postpartum fat mass retention (B's = 0.04 to 0.18, 95%CIs: 0.001, 0.32). Further, the mixture of EDCs was positively associated with late pregnancy fat mass gain. Conclusion: In this cohort, pre-pregnancy BMI was a key determinant of the associations between second trimester exposure to bisphenols and phthalates and maternal weight changes and fat accumulation. Investigations of underlying physiological mechanisms, windows of susceptibility, and impacts on maternal and infant health are needed.
https://doi.org/10.1016/j.envres.2024.119276

Metal and oxidative potential exposure through particle inhalation and oxidative stress biomarkers: a 2-week pilot prospective study among Parisian subway workers,
SAUVAIN J.-J., M. HEMMENDINGER, T. CHARREAU, V. JOUANNIQUE, A. DEBATISSE, G. SUÁREZ, N. B. HOPF and I. GUSEVA CANU, *International Archives of Occupational and Environmental Health* 97, no. 4 (2024/05/01 2024): 387-400,
In this pilot study on subway workers, we explored the relationships between particle exposure and oxidative stress biomarkers in exhaled breath condensate (EBC) and urine to identify the most relevant biomarkers for a large-scale study in this field. https://doi.org/10.1007/s00420-024-02054-2

Per- and polyfluoroalkyl substances (PFAS) and fetal growth: A nation-wide register-based study on PFAS in drinking water,
SÄVE-SÖDERBERGH M., I. GYLLENHAMMAR, T. SCHILLEMANS, E. LINDFELDT, C. VOGS, C. DONAT-VARGAS, E. H. ANKARBERG, A. GLYNN, L. AHRENS, E. HELTE and A. ÅKESSON, *Environment International* 187 (May 2024),
Background: There is inconclusive evidence for an association between per- and polyfluoroalkyl substances (PFAS) and fetal growth. Objectives: We conducted a nation-wide register-based cohort

study to assess the associations of the estimated maternal exposure to the sum (PFAS4) of perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA) and perfluorohexane sulfonic acid (PFHxS) with birthweight as well as risk of small- (SGA) and large-for-gestational-age (LGA). Materials and methods: We included all births in Sweden during 2012-2018 of mothers residing >= four years prior to partus in localities served by municipal drinking water where PFAS were measured in raw and drinking water. Using a one-compartment toxicokinetic model we estimated cumulative maternal blood levels of PFAS4 during pregnancy by linking residential history, municipal PFAS water concentration and year-specific background serum PFAS concentrations in Sweden. Individual birth outcomes and covariates were obtained via register linkage. Mean values and 95 % confidence intervals (CI) of beta coefficients and odds ratios (OR) were estimated by linear and logistic regressions, respectively. Quantile g-computation regression was conducted to assess the impact of PFAS4 mixture. Results: Among the 248,804 singleton newborns included, no overall association was observed for PFAS4 and birthweight or SGA. However, an association was seen for LGA, multivariable-adjusted OR 1.08 (95% CI: 1.01-1.16) when comparing the highest PFAS4 quartile to the lowest. These associations remained for mixture effect approach where all PFAS, except for PFOA, contributed with a positive weight. Discussions: We observed an association of the sum of PFAS4 - especially PFOS - with increased risk of LGA, but not with SGA or birthweight. The limitations linked to the exposure assessment still require caution in the interpretation. https://doi.org/10.1016/j.envint.2024.108727

Pesticide exposure and increased breast cancer risk in women population studies,
PANIS C. and B. LEMOS, *Science of the Total Environment* 933 (Jul 2024),
Pesticide exposure is emerging as a risk factor for various human diseases. Breast cancer (BC) is a multifactorial disease with known genetic and non-genetic risk factors. Most BC cases are attibutable to non-genetic risk factors, with a history of adverse environmental exposures playing a significant role. Pesticide exposure can occur at higher levels in female populations participating in rural activities such as spraying of pesticides in the field, unprotected handling of pesticides at home, and washing of contaminated clothes. Exposure can also be significant in the drinking water of certain populations. Here, we reviewed the literature on women's exposure to pesticides and the risk of BC. We summarize the main links between pesticide exposure and BC and discuss the role of dose and exposure context, as well as potential mechanisms of toxicity. Overall, reports reviewed here have documented stronger associations between higher levels of exposure and BC risk, including documenting direct and acute pesticide exposure in certain female populations. However, discrepancies among studies regarding dose and mode of exposure may result in misunderstandings about the risks posed by pesticide exposure. Plausible mechanisms linking pesticides to breast cancer risk include their impacts as endocrine disruptors, as well as their roles as genotoxic agents, and modulators of the epigenome. Besides establishing links between pesticide exposure and breast cancer, the literature also highlights the critical need to understand the routes and doses of women's exposure to pesticides and the specific associations and mechanisms that are determinants of disease etiology and prognosis.
https://doi.org/10.1016/j.scitotenv.2024.172988

Phthalates and sex steroid hormones across the perimenopausal period: A longitudinal analysis of the Midlife Women's Health Study,
BABADI R. S., P. L. WILLIAMS, E. V. PRESTON, Z. LI, R. L. SMITH, R. S. STRAKOVSKY, S. MAHALINGAIAH, R. HAUSER, J. A. FLAWS and T. J. TODD, *Environment International* 188 (Jun 2024),
Background: The menopausal transition involves significant sex hormone changes. Environmental chemicals, such as urinary phthalate metabolites, are associated with sex hormone levels in cross-

sectional studies. Few studies have assessed longitudinal associations between urinary phthalate metabolite concentrations and sex hormone levels during menopausal transition. Methods: Pre- and perimenopausal women from the Midlife Women's Health Study (MWHS) (n = 751) contributed data at up to 4 annual study visits. We quantified 9 individual urinary phthalate metabolites and 5 summary measures (e.g., phthalates in plastics (EPlastic)), using pooled annual urine samples. We measured serum estradiol, testosterone, and progesterone collected at each study visit, unrelated to menstrual cycling. Linear mixed-effects models and hierarchical Bayesian kernel machine regression analyses evaluated adjusted associations between individual and phthalate mixtures with sex steroid hormones longitudinally. Results: We observed associations between increased concentrations of certain phthalate metabolites and lower testosterone and higher sub-ovulatory progesterone levels, e.g., doubling of monoethyl phthalate (MEP), monobenzyl phthalate (MBzP), di-2-ethylhexyl phthalate (EDEHP) metabolites, EPlastic, and EPhthalates concentrations were associated with lower testosterone (e.g., for EDEHP: -4.51%; 95% CI: -6.72%, -2.26%). For each doubling of MEP, certain DEHP metabolites, and summary measures, we observed higher mean subovulatory progesterone (e.g., EAA (metabolites with anti-androgenic activity): 6.88%; 95% CI: 1.94%, 12.1%). Higher levels of the overall time-varying phthalate mixture were associated with lower estradiol and higher progesterone levels, especially for 2nd year exposures. Conclusions: Phthalates were longitudinally associated with sex hormone levels during the menopausal transition. Future research should assess such associations and potential health impacts during this understudied period. https://doi.org/10.1016/j.envint.2024.108770

Plastic-related endocrine disrupting chemicals significantly related to the increased risk of estrogen-dependent diseases in women,
CHITAKWA N., M. ALQUDAIMI, M. SULTAN and D. WU, *Environmental Research* 252 (Jul 2024), Objective: To evaluate the association between exposure to plastic-related endocrine-disrupting chemicals (EDCs), specifically Bisphenol A (BPA), Phthalates, Cadmium, and Lead, and the risk of estrogen-dependent diseases (EDDs) such as polycystic ovary syndrome (PCOS), endometriosis, or endometrial cancer by conducting a metaanalysis of relevant studies. Methods: PubMed, Web of Science, and Cochrane Library databases were used for literature retrieval of articles published until the 21st of April 2023. Literature that evaluated the association between BPA, phthalates, cadmium, and/or lead exposure and the risk of PCOS, endometriosis, or endometrial cancer development or exacerbation were included in our analysis. STATA/MP 17.0 was used for all statistical analyses. Results: Overall, 22 articles were included in our meta-analysis with a total of 83,641 subjects all of whom were females aged between 18 and 83 years old. The overall effect size of each study was as follows: endometriosis risk in relation to BPA exposure ES 1.82 (95% CI; 1.50, 2.20). BPA and PCOS risk ES 1.61 (95% CI; 1.39, 1.85). Phthalate metabolites and endometriosis risk; MBP ES 1.07 (95% CI; 0.86, 1.33), MEP ES 1.05 (95% CI; 0.87, 1.28), MEHP ES 1.15 (95% CI; 0.67, 1.98), MBzP ES 0.97 (95% CI; 0.63, 1.49), MEOHP ES 1.87 (95% CI; 1.21, 2.87), and MEHHP ES 1.98 (95% CI; 1.32, 2.98). Cadmium exposure and endometrial cancer risk ES 1.14 (95% CI; 0.92, 1.41). Cadmium exposure and the risk of endometriosis ES 2.54 (95% CI; 1.71, 3.77). Lead exposure and the risk of endometriosis ES 1.74 (95% CI; 1.13, 2.69). Conclusion: Increased serum, urinary, or dietary concentration of MBzP and MEHP in women is significantly associated with endometriosis risk. Increased cadmium concentration is associated with endometrial cancer risk. https://doi.org/10.1016/j.envres.2024.118966

The potential Association of Bisphenol A exposure and type 1 diabetes mellitus among Dakahlia Governorate's children sample, Egypt,
EL-DEGWI B. A. A., M. E. AWAD, W. LAIMON, S. A. ASKAR, D. A. W. EL-MORSI and D. A. M. AHMED, *Toxicol Res (Camb)* 13, no. 3 (Jun 2024): tfae093,

BACKGROUND: Bisphenol A (BPA) is an endocrine disrupter affecting glucose homeostasis. OBJECTIVES: This study aimed to investigate BPA's relationship with Type 1 Diabetes Mellitus (T1DM) in Dakahlia Governorate's children, in Egypt. SUBJECTS MATERIALS AND METHODS: The study had two parts: clinical and experimental. Clinical Study was conducted on 200 children, equally divided into control and T1DM groups. They underwent: demographic data, height, weight, body mass index, glycosylated HbA1C, random blood glucose, and urinary BPA measurements. Experimental Study was conducted on 60 adult albino rats. Rats were randomly divided into three equal groups: control group: received 0.5 mL of pure olive oil, group 1: received 20 mg/kg/day BPA, and group 2: received 100 mg/kg/day BPA orally for 6 weeks. Fasting and two hours postprandial glucose levels were measured at the beginning and end of the study. Histopathological examination and imaging study of the pancreas were done. RESULTS: In clinical study: HbA1C and random blood glucose levels in diabetic children showed a significant increase compared to control. Children in control group showed controlled HbA1C, while the T1DM group showed 86% with poor diabetic control. There was a significant increase in BPA level in the T1DM group compared to the control. Rats that received BPA showed a marked increase in fasting and two hours postprandial glucose levels, histopathological changes in the pancreas with more changes determined in the high dose group, and a significant decrease in the islets of Langerhans diameters with group 2 more affected. CONCLUSION: So, BPA exposure could be considered a risk factor for T1DM in children. https://doi.org/10.1093/toxres/tfae093

Prenatal exposure to benzophenone-type UV filters and the associations with neonatal birth outcomes and maternal health in south China,
FU J. F., Y. YAO, Z. H. HUANG, J. Y. HUANG, D. ZHANG, X. Y. LI, J. Y. XU, Q. R. XIAO and S. Y. LU, *Environment International* 189 (Jul 2024),
Benzophenone (BP)-type UV filters are commonly added to sunscreens and cosmetics to protect against UV radiation for human skin and hair. As a result, BPs are ubiquitous in the environment and human body, and their endocrine-disrupting characteristics have been a hot topic of discussion. However, our knowledge regarding the detrimental effects of prenatal exposure to BPs on pregnant women and their offspring remains limited. To fill this gap, we determined five BP derivatives in 600 serum samples obtained from pregnant women. All the target analytes, except 2,4-dihydroxybenzophenone (BP-1), have achieved a 100 % detection rate. The most prevalent compound was 2-hydroxy-4-methoxybenzophenone (BP-3), with a median concentration of 0.545 ng/mL. Significant and positive correlations were observed among BP derivatives, indicating both endogenous metabolism and common external sources. Utilizing Bayesian kernel machine regression (BKMR) and quantile-based gcomputation (QGC) models, we found relationships between BP exposure and reduced neonatal birth weight (BW) and birth chest circumference (BC) during the third trimester. Notably, the adverse effect of BPs on birth size was sex-specific. Moreover, triglyceride (TG) was identified as a potential mediator of the effect of BPs on blood pressure, and co-exposure to BPs was linked to disruptions in thyroid hormone levels and glucose regulation. Further research is warranted to unravel the toxicity of BPs and their detrimental effects on pregnant women and fetuses. https://doi.org/10.1016/j.envint.2024.108797

Prenatal Exposure to Chemical Mixtures and Metabolic Syndrome Risk in Children,
GÜIL-OUMRAIT N., N. STRATAKIS, L. MAITRE, A. ANGUITA-RUIZ, J. URQUIZA, L. FABBRI, X. BASAGAÑA, B. HEUDE, L. S. HAUG, A. K. SAKHI, N. ISZATT, H. C. KEUN, J. WRIGHT, L. CHATZI, M. VAFEIADI, M. BUSTAMANTE, R. GRAZULEVICIENE, S. ANDRUŠAITYTĖ, R. SLAMA, R. MCEACHAN, M. CASAS and M. VRIJHEID, *JAMA Network Open* 7, no. 5 (2024): e2412040-e2412040,
Prenatal exposure to ubiquitous endocrine-disrupting chemicals (EDCs) may increase the risk of metabolic syndrome (MetS) in children, but few studies have studied chemical mixtures or explored underlying protein and metabolic signatures.To investigate associations of prenatal exposure to

EDC mixtures with MetS risk score in children and identify associated proteins and metabolites.This population-based, birth cohort study used data collected between April 1, 2003, and February 26, 2016, from the Human Early Life Exposome cohort based in France, Greece, Lithuania, Norway, Spain, and the UK. Eligible participants included mother-child pairs with measured prenatal EDC exposures and complete data on childhood MetS risk factors, proteins, and metabolites. Data were analyzed between October 2022 and July 2023.Nine metals, 3 organochlorine pesticides, 5 polychlorinated biphenyls, 2 polybrominated diphenyl ethers (PBDEs), 5 perfluoroalkyl substances (PFAS), 10 phthalate metabolites, 3 phenols, 4 parabens, and 4 organophosphate pesticide metabolites measured in urine and blood samples collected during pregnancy.At 6 to 11 years of age, a composite MetS risk score was constructed using z scores of waist circumference, systolic and diastolic blood pressures, triglycerides, high-density lipoprotein cholesterol, and insulin levels. Childhood levels of 44 urinary metabolites, 177 serum metabolites, and 35 plasma proteins were quantified using targeted methods. Associations were assessed using bayesian weighted quantile sum regressions applied to mixtures for each chemical group.The study included 1134 mothers (mean [SD] age at birth, 30.7 [4.9] years) and their children (mean [SD] age, 7.8 [1.5] years; 617 male children [54.4%] and 517 female children [45.6%]; mean [SD] MetS risk score, −0.1 [2.3]). MetS score increased per 1-quartile increase of the mixture for metals (β = 0.44; 95% credible interval [CrI], 0.30 to 0.59), organochlorine pesticides (β = 0.22; 95% CrI, 0.15 to 0.29), PBDEs (β = 0.17; 95% CrI, 0.06 to 0.27), and PFAS (β = 0.19; 95% CrI, 0.14 to 0.24). High-molecular weight phthalate mixtures (β = −0.07; 95% CrI, −0.10 to −0.04) and low-molecular weight phthalate mixtures (β = −0.13; 95% CrI, −0.18 to −0.08) were associated with a decreased MetS score. Most EDC mixtures were associated with elevated proinflammatory proteins, amino acids, and altered glycerophospholipids, which in turn were associated with increased MetS score.This cohort study suggests that prenatal exposure to EDC mixtures may be associated with adverse metabolic health in children. Given the pervasive nature of EDCs and the increase in MetS, these findings hold substantial public health implications. https://doi.org/10.1001/jamanetworkopen.2024.12040

Prevalence and implications of microplastic contaminants in general human seminal fluid: A Raman spectroscopic study,
LI N., H. J. YANG, Y. L. DONG, B. WEI, L. Y. LIANG, X. YUN, J. Q. TIAN, Y. F. ZHENG, S. Y. DUAN and L. ZHANG, *Science of the Total Environment* 937 (Aug 2024),
Microplastics are ubiquitous environmental contaminants that have been detected in human semen from polluted areas, yet their prevalence and effects in the general population remain largely unexplored. To examine microplastic presence, abundance, polymer types, and associations with semen quality parameters in individuals without occupational exposures, this study was conducted by collecting semen samples from 40 participants undergoing premarital health assessments in Jinan, China. Raman microspectroscopy was employed to identify, quantify, and categorize microplastic polymers, sperm motility was assessed via computer-assisted analysis, and morphology was evaluated through Diff-Quik staining. Correlations between demographics, semen parameters, and microplastic content were examined by statistical analysis. We found that microplastics were detected in all semen samples, with 2 particles per sample (ranging from 0.72 to 7.02 mu m). Eight distinct polymers were identified, with polystyrene (31 %) being most prevalent. Semen exposed to polystyrene demonstrated higher sperm progressive motility as compared to polyvinyl chloride exposure group (43.52 +/- 14.21 % vs 19.04 +/- 13.46 %). Sperm morphological abnormalities were observed but not significantly associated with specific plastic types. In conclusion, this study reveals microplastic contamination in semen from individuals without occupational exposure, with PS, PE, and PVC being the most prevalent and exhibiting differential correlations with sperm progressive motility, and highlight the need for further research into the potential reproductive impacts of microplastic exposure.
https://doi.org/10.1016/j.scitotenv.2024.173522

The relationship between bisphenol A and phthalates with precocious puberty in Vietnamese children,
HUYNH Q. T. V., H. T. BAN, N. L. VUONG and N. P. KHANH, *Journal of Pediatric Endocrinology & Metabolism* (2024 Jun 2024),
Objectives This study is aimed to explore the correlation between bisphenol A (BPA) and phthalates, including diethylhexylphthalate (DEHP) and dibutylphthalate (DBP), and precocious puberty (PP). Methods A case-control study was conducted in Ho Chi Minh City, Vietnam, from November 2021 to April 2022, involving 250 children, with 124 of them diagnosed with PP and 126 serving as controls. We assessed the levels of urinary BPA, DEHP, and DBP in all participants and examined their association with the risk of PP. Results BPA was detected in 11.3 % of PP cases but was not found in any individuals in the control group (p<0.001). Diethylhexylphthalate metabolite (MEHP) was not detected in any of the samples. Positive urinary results for dibutylphthalate metabolite (MBP) were observed in 8.1 % of PP cases and 2.4 % in the control group, with an odds ratio of 3.6 (95 % confidence interval: 0.97-13.4, p=0.03). Conclusions The PP group exhibited a higher prevalence of positive urinary BPA and DBP levels compared to the control group.
https://doi.org/10.1515/jpem-2024-0144

A Review of the Association between Exposure to Flame Retardants and Thyroid Function,
YESHOUA B., H. ROMERO CASTILLO, M. MONAGHAN and M. VAN GERWEN, *Biomedicines* 12, no. 6 (Jun 19 2024),
Flame retardants have been shown to cause widespread physiological effects, in particular on endocrine organs such as the thyroid. This review aims to provide an overview of the literature on the association between flame retardants and thyroid function within humans. A search in the National Library of Medicine and National Institutes of Health PubMed database through January 2024 yielded 61 studies that met the inclusion criteria. The most frequently analyzed flame retardants across all thyroid hormones were polybrominated diphenyl ethers (PBDEs), in particular BDE-47 and BDE-99. Ten studies demonstrated exclusively positive associations between flame retardants and thyroid stimulating hormone (TSH). Six studies demonstrated exclusively negative associations between flame retardants and TSH. Twelve studies demonstrated exclusively positive associations for total triiodothyronine (tT3) and total thyroxine (tT4). Five and eight studies demonstrated exclusively negative associations between flame retardants and these same thyroid hormones, respectively. The effect of flame retardants on thyroid hormones is heterogeneous; however, the long-term impact warrants further investigation. Vulnerable populations, including indigenous people, individuals working at e-waste sites, firefighters, and individuals within certain age groups, such as children and elderly, are especially critical to be informed of risk of exposure.
https://doi.org/10.3390/biomedicines12061365

Sex and adrenal hormones in association with insecticide biomarkers among adolescents living in ecuadorian agricultural communities,
CHRONISTER B. N. C., D. JUSTO, R. J. WOOD, D. LOPEZ-PAREDES, E. GONZALEZ, J. SUAREZ-TORRES, S. GAHAGAN, D. MARTINEZ, D. R. JACOBS, JR., H. CHECKOWAY, M. M. JANKOWSKA and J. R. SUAREZ-LOPEZ, *International Journal of Hygiene and Environmental Health* 259 (Jun 2024),
Background: Organophosphate, pyrethroid, and neonicotinoid insecticides have resulted in adrenal and gonadal hormone disruption in animal and in vitro studies; limited epidemiologic evidence exists in humans. We assessed relationships of urinary insecticide metabolite concentrations with adrenal and gonadal hormones in adolescents living in Ecuadorean agricultural communities. Methods: In 2016, we examined 522 Ecuadorian adolescents (11-17y, 50.7% female, 22% Indigenous; ESPINA study). We measured urinary insecticide metabolites, blood acetylcholinesterase activity (AChE), and salivary testosterone, dehydroepiandrosterone (DHEA),

1713-estradiol, and cortisol. We used general linear models to assess linear (13 = % hormone difference per 50% increase of metabolite concentration) and curvilinear relationships (13 2 = hormone difference per unit increase in squared ln-metabolite) between ln-metabolite or AChE and ln-hormone concentrations, stratified by sex, adjusting for anthropometric, demographic, and awakening response variables. Bayesian Kernel Machine Regression was used to assess non-linear associations and interactions. Results: The organophosphate metabolite malathion dicarboxylic acid (MDA) had positive associations with testosterone (13 boys = 5.88% [1.21%, 10.78%], 13 girls = 4.10% [-0.02%, 8.39%]), and cortisol (13 boys = 6.06 [-0.23%, 12.75%]. Paranitrophenol (organophosphate) had negatively -trending curvilinear associations, with testosterone (13 2 boys = -0.17 (-0.33, -0.003), p = 0.04) and DHEA (13 2 boys = -0.49 (-0.80, -0.19), p = 0.001) in boys. The neonicotinoid summary score (13 boys = 5.60% [0.14%, 11.36%]) and the neonicotinoid acetamiprid-Ndesmethyl (13 boys = 3.90% [1.28%, 6.58%]) were positively associated with 1713-estradiol, measured in boys only. No associations between the pyrethroid 3-phenoxybenzoic acid and hormones were observed. In girls, bivariate response associations identified interactions of MDA, Paranitrophenol, and 3,5,6-trichloro-2-pyridinol (organophosphates) with testosterone and DHEA concentrations. In boys, we observed an interaction of MDA and Paranitrophenol with DHEA. No associations were identified for AChE. Conclusions: We observed evidence of endocrine disruption for specific organophosphate and neonicotinoid metabolite exposures in adolescents. Urinary organophosphate metabolites were associated with testosterone and DHEA concentrations, with stronger associations in boys than girls. Urinary neonicotinoids were positively associated with 1713-estradiol. Longitudinal repeat -measures analyses would be beneficial for causal inference. https://doi.org/10.1016/j.ijheh.2024.114386

Toxic impacts of arsenic bioaccumulation on urinary arsenic metabolites and semen quality: A systematic and meta-analysis,
AKHIGBE R. E., T. M. AKHIGBE, C. A. ADEGBOLA, P. A. OYEDOKUN, O. B. ADESOYE and A. E. ADEOGUN, *Ecotoxicol Environ Saf* 281 (Jun 27 2024): 116645,
This study aims to investigate the effect of arsenic exposure on urinary levels of arsenic metabolites, semen parameters, and testosterone concentrations. A systematic comprehensive literature search was conducted up till 31st January 2024 using Embase, MEDLINE/Pubmed, and Scopus. This study adopted the Population Exposure Comparator Outcome and Study Design (PECOS) framework. Four studies with a total of 380 control subjects and 347 exposed men were included. Arsenic exposure significantly increased urinary levels of total arsenic (Mean Difference (MD) - 53.35 [95 % Confidence Interval (CI): - 100.14, - 6.55] P= 0.03), and reduced primary arsenic methylation index (PMI) (MD 0.22 [95 % CI: 0.14, 0.31] P< 0.00001), semen volume (MD 0.30 [95 % CI: 0.05, 0.54] P= 0.02) and total testosterone (MD 0.48 [95 % CI: 0.23, 0.73] P= 0.0002). In addition, arsenic exposure marginally reduced sperm concentration (MD 25.04 [95 % CI: - 45.42, 95.50] P= 0.49) and total sperm motility (MD 22.89 [95 % CI: - 14.15, 59.94] P= 0.23). The present meta-analysis demonstrates that arsenic exposure lowers semen quality and testosterone levels. Since the general human population is exposed to arsenic occupationally or domestically, adequate strategic measures should be put in place to limit arsenic exposure in an attempt to preserve semen quality. In addition, studies investigating interventions that may inhibit the bioaccumulation of arsenic in men who are exposed are recommended.
https://doi.org/10.1016/j.ecoenv.2024.116645

Toxicité sur l'homme

Advances in understanding the reproductive toxicity of endocrine-disrupting chemicals in women,
WANG J. G., C. W. ZHAO, J. FENG, P. P. SUN, Y. H. ZHANG, A. L. HAN, Y. M. ZHANG and H. G. MA, *Frontiers in Cell and Developmental Biology* 12 (Mar 2024),
Recently, there has been a noticeable increase in disorders of the female reproductive system, accompanied by a rise in adverse pregnancy outcomes. This trend is increasingly being linked to environmental pollution, particularly through the lens of Endocrine Disrupting Chemicals (EDCs). These external agents disrupt natural processes of hormones, including synthesis, metabolism, secretion, transport, binding, as well as elimination. These disruptions can significantly impair human reproductive functions. A wealth of animal studies and epidemiological research indicates that exposure to toxic environmental factors can interfere with the endocrine system's normal functioning, resulting in negative reproductive outcomes. However, the mechanisms of these adverse effects are largely unknown. This work reviews the reproductive toxicity of five major environmental EDCs-Bisphenol A (BPA), Phthalates (PAEs), Triclocarban Triclosan and Disinfection Byproducts (DBPs)-to lay a foundational theoretical basis for further toxicological study of EDCs. Additionally, it aims to spark advancements in the prevention and treatment of female reproductive toxicity caused by these chemicals. https://doi.org/10.3389/fcell.2024.1390247

Bisphenol A (BPA) and neurological disorders: An overview,
HYUN S. A. and M. KA, *Int J Biochem Cell Biol* 173 (Jun 27 2024): 106614,
The human body is commonly exposed to bisphenol A (BPA), which is widely used in consumer and industrial products. BPA is an endocrine-disrupting chemical that has adverse effects on human health. In particular, many studies have shown that BPA can cause various neurological disorders by affecting brain development and neural function during prenatal, infancy, childhood, and adulthood exposure. In this review, we discussed the correlation between BPA and neurological disorders based on molecular cell biology, neurophysiology, and behavioral studies of the effects of BPA on brain development and function. Recent studies, both animal and epidemiological, strongly indicate that BPA significantly impacts brain development and function. It hinders neural processes, such as proliferation, migration, and differentiation during development, affecting synaptic formation and activity. As a result, BPA is implicated in neurodevelopmental and neuropsychiatric disorders like autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), and schizophrenia. https://doi.org/10.1016/j.biocel.2024.106614

Cyanotoxin cylindrospermopsin disrupts lipid homeostasis and metabolism in a 3D in vitro model of the human liver,
CHOWDHURY R. R., M. F. GROSSO, D. C. GADARA, Z. SPÁČIL, V. VIDOVÁ, I. SOVADINOVÁ and P. BABICA, *Chemico-Biological Interactions* 397 (2024/07/01/ 2024): 111046,
Cylindrospermopsin, a potent hepatotoxin produced by harmful cyanobacterial blooms, poses environmental and human health concerns. We used a 3D human liver in vitro model based on spheroids of HepG2 cells, in combination with molecular and biochemical assays, automated imaging, targeted LC-MS-based proteomics, and lipidomics, to explore cylindrospermopsin effects on lipid metabolism and the processes implicated in hepatic steatosis. Cylindrospermopsin (1 µM, 48 h) did not significantly affect cell viability but partially reduced albumin secretion. However, it increased neutral lipid accumulation in HepG2 spheroids while decreasing phospholipid levels. Simultaneously, cylindrospermopsin upregulated genes for lipogenesis regulation (SREBF1) and triacylglycerol synthesis (DGAT1/2) and downregulated genes for fatty acid synthesis (ACLY, ACCA, FASN, SCD1). Fatty acid uptake, oxidation, and lipid efflux genes were not significantly affected. Targeted proteomics revealed increased levels of perilipin 2 (adipophilin), a major hepatocyte lipid

droplet-associated protein. Lipid profiling quantified 246 lipid species in the spheroids, with 28 significantly enriched and 15 downregulated by cylindrospermopsin. Upregulated species included neutral lipids, sphingolipids (e.g., ceramides and dihexosylceramides), and some glycerophospholipids (phosphatidylethanolamines, phosphatidylserines), while phosphatidylcholines and phosphatidylinositols were mostly reduced. It suggests that cylindrospermopsin exposures might contribute to developing and progressing towards hepatic steatosis or metabolic dysfunction-associated steatotic liver disease (MASLD).
https://doi.org/10.1016/j.cbi.2024.111046

Effects of pharmaceutical and personal care products on pubertal development: Evidence from human and animal studies,
WANG L. P., X. Q. YE and J. LIU, *Environmental Pollution* 346 (Apr 2024),
Pharmaceutical and personal care products (PPCPs) include a wide range of drugs, personal care products and household chemicals that are produced and used in significant quantities. The safety of PPCPs has become a growing concern in recent decades due to their ubiquitous presence in the environment and potential risks to human health. PPCPs have been detected in various human biological samples, including those from children and adolescents, at concentrations ranging from several ng/L to several thousand mu g/L. Epidemiological studies have shown associations between exposure to PPCPs and changes in the timing of puberty in children and adolescents. Animal studies have shown that exposure to PPCPs results in advanced or delayed pubertal onset. Mechanisms by which PPCPs regulate pubertal development include alteration of the hypothalamic kisspeptin and GnRH networks, disruption of steroid hormones, and modulation of metabolic function and epigenetics. Gaps in knowledge and further research needs include the assessment of environmental exposure to pharmaceuticals in children and adolescents, low-dose and long-term effects of exposure to PPCPs, and the modes of action of PPCPs on pubertal development. In summary, this comprehensive review examines the potential effects of exposure to PPCPs on pubertal development based on evidence from human and animal studies.
https://doi.org/10.1016/j.envpol.2024.123533

Emerging regulatory roles of noncoding RNAs induced by bisphenol A (BPA) and its alternatives in human diseases,
HE B., H. M. XU, S. W. LI, Y. F. ZHANG and J. W. TIAN, *Environ Pollut* (Jun 26 2024): 124447,
Bisphenols (BPs), including BPA, BPF, BPS, and BPAF, are synthetic phenolic organic compounds and endocrine-disrupting chemicals. These organics have been broadly utilized to produce epoxy resins, polycarbonate plastics, and other products. Mounting evidence has shown that BPs, especially BPA, may enter into the human body and participate in the development of human diseases mediated by nuclear hormone receptors. Moreover, BPA may negatively affect human health at the epigenetic level through processes such as DNA methylation and histone acetylation. Recent studies have demonstrated that, as part of epigenetics, noncoding RNAs (ncRNAs), including microRNAs (miRNAs), long noncoding RNAs (lncRNAs), circular RNAs (circRNAs), and small nucleolar RNAs (snoRNAs), have vital impacts on BP-related diseases, such as reproductive system diseases, nervous system diseases, digestive system diseases, endocrine system diseases, and other diseases. Moreover, based on the bioinformatic analysis, changes in ncRNAs may be relevant to normal activities and functions and BP-induced diseases. Thus, we conducted a meta-analysis to identify more promising ncRNAs as biomarkers and therapeutic targets for BP exposure and relevant human diseases. In this review, we summarize the regulatory functions of ncRNAs induced by BPs in human diseases and latent molecular mechanisms, as well as identify prospective biomarkers and therapeutic targets for BP exposure and upper diseases.
https://doi.org/10.1016/j.envpol.2024.124447

Endocrine disrupting chemicals: gestational diabetes and beyond,
MITRA T., R. GULATI, K. RAMACHANDRAN, R. RAJIV, E. A. L. ENNINGA, C. K. PIERRET, R. S. KUMARI and R. JANARDHANAN, *Diabetology & Metabolic Syndrome* 16, no. 1 (Apr 2024),
Gestational Diabetes Mellitus (GDM) has been on the rise for the last two decades along with the growing incidence of obesity. The ubiquitous use of Endocrine-Disrupting Chemicals (EDCs) worldwide has been associated with this increase in GDM incidence. Epigenetic modifications such as DNA methylation, histone acetylation, and methylation have been associated with prenatal exposure to EDCs. EDC exposure can also drive a sustained disruption of the hypothalamus-pituitary-thyroid axis and various other signaling pathways such as thyroid signaling, PPAR gamma signaling, PI3K-AKT signaling. This disruption leads to impaired glucose metabolism, insulin resistance as well as beta-cell dysfunction, which culminate into GDM. Persistent EDC exposure in pregnant women also increases adipogenesis, which results in gestational weight gain. Importantly, pregnant mothers transfer these EDCs to the fetus via the placenta, thus leading to other pregnancy-associated complications such as intrauterine growth restriction (IUGR), and large for gestational age neonates. Furthermore, this early EDC exposure of the fetus increases the susceptibility of the infant to metabolic diseases in early life. The transgenerational impact of EDCs is also associated with higher vascular tone, cognitive aberrations, and enhanced susceptibility to lifestyle disorders including reproductive health anomalies. The review focuses on the impact of environmental toxins in inducing epigenetic alterations and increasing the susceptibility to metabolic diseases during pregnancy needs to be extensively studied such that interventions can be developed to break this vicious cycle. Furthermore, the use of EDC-associated ExomiRs from the serum of patients can help in the early diagnosis of GDM, thereby leading to triaging of patients based on increasing risk factor of the clinicopathological condition.
https://doi.org/10.1186/s13098-024-01317-9

Endocrine disrupting potential of total and bioaccessible extracts of dust from seven different types of indoor environment,
PINTO-VIDAL F. A., J. NOVÁK, S. R. JILKOVÁ, T. RUSINA, B. VRANA, L. MELYMUK and K. HILSCHEROVÁ, *Journal of Hazardous Materials* 469 (May 2024),
exposure potential mostly limited to a few pollutant groups and indoor types. This study provides a comprehensive toxicological profile of chemical mixtures associated with dust from various types of indoor environments, namely cars, houses, prefabricated apartments, kindergartens, offices, public spaces, and schools. Organic extracts of two different polarities and bioaccessible extracts mimicking the gastrointestinal conditions were prepared from two different particle size fractions of dust. These extracts were tested on a battery of human cell -based bioassays to assess endocrine disrupting potentials. Furthermore, 155 chemicals from different pollutant groups were measured and their relevance for the bioactivity was determined using concentration addition modelling. The exhaustive and bioaccessible extracts of dust from the different microenvironments interfered with aryl hydrocarbon receptor, estrogen, androgen, glucocorticoid, and thyroid hormone (TH) receptor signalling, and with TH transport. Noteably, bioaccessible extracts from offices and public spaces showed higher estrogenic effects than the organic solvent extracts. 114 of the 155 targeted chemicals were detectable, but the observed bioactivity could be only marginally explained by the detected chemicals. Diverse toxicity patterns across different microenvironments that people inhabit throughout their lifetime indicate potential health and developmental risks, especially for children. Limited data on the endocrine disrupting potency of relevant chemical classes, especially those deployed as replacements for legacy contaminants, requires further study.
https://doi.org/10.1016/j.jhazmat.2024.133778

Exploring novel insights into the molecular mechanisms underlying Bisphenol A-induced toxicity: A persistent threat to human health,

AHMAD I., M. KAUR, D. TYAGI, T. B. SINGH, G. KAUR, S. M. AFZAL and M. JAUHAR, *Environmental Toxicology and Pharmacology* 108 (Jun 2024),
Bisphenol A (BPA) is a ubiquitous industrial chemical used in the production of polycarbonate plastics and epoxy resins, found in numerous consumer products. Despite its widespread use, its potential adverse health effects have raised significant concerns. This review explores the molecular mechanisms and evidence-based literature underlying BPA-induced toxicities and its implications for human health. BPA is an endocrine-disrupting chemical (EDC) which exhibits carcinogenic properties by influencing various receptors, such as ER, AhR, PPARs, LXRs, and RARs. It induces oxidative stress and contributes to cellular dysfunction, inflammation, and DNA damage, ultimately leading to various toxicities including but not limited to reproductive, cardiotoxicity, neurotoxicity, and endocrine toxicity. Moreover, BPA can modify DNA methylation patterns, histone modifications, and non-coding RNA expression, leading to epigenetic changes and contribute to carcinogenesis. Overall, understanding molecular mechanisms of BPA-induced toxicity is crucial for developing effective strategies and policies to mitigate its adverse effects on human health. https://doi.org/10.1016/j.etap.2024.104467

Exposure to the phthalate metabolite MEHP impacts survival and growth of human ovarian follicles in vitro,
PANAGIOTOU E. M., A. DAMDIMOPOULOS, T. Y. LI, E. MOUSSAUD-LAMODIÈRE, M. PEDERSEN, F. LEBRE, K. PETTERSSON, C. ARNELO, K. PAPAIKONOMOU, E. ALFARO-MORENO, C. LINDSKOG, T. SVINGEN and P. DAMDIMOPOULOU, *Toxicology* 505 (Jun 2024),
Phthalates are found in everyday items like plastics and personal care products. There is an increasing concern that continuous exposure can adversely affect female fertility. However, experimental data are lacking to establish causal links between exposure and disease in humans. To address this gap, we tested the effects of a common phthalate metabolite, mono-(2-ethylhexyl) phthalate (MEHP), on adult human ovaries in vitro using an epidemiologically determined human -relevant concentration range (2.05 nM - 20.51 mM). Histomorphological assessments, steroid and cytokine measurements were performed on human ovarian tissue exposed to MEHP for 7 days in vitro . Cell viability and gene expression profile were investigated following 7 days of MEHP exposure using the human granulosa cancer cell lines KGN, and COV434, the germline tumor cell line PA -1, and human ovarian primary cells. Selected differentially expressed genes (DEGs) were validated by RT-qPCR and immunofluorescence in human ovarian tissue. MEHP exposure reduced follicular growth (20.51 nM) and increased follicular degeneration (20.51 mM) in ovarian tissue, while not affecting steroid and cytokine production. Out of the 691 unique DEGs identified across all the cell types and concentrations, CSRP2 involved in cytoskeleton organization and YWHAE as well as CTNNB1 involved in the Hippo pathway, were chosen for further validation. CSRP2 was upregulated and CTNNB1 downregulated in both ovarian tissue and cells, whereas YWHAE was downregulated in cells only. In summary, one -week MEHP exposure of human ovarian tissue can perturb the development and survival of human follicles through mechanisms likely involving dysregulation of cytoskeleton organization and Hippo pathway.
https://doi.org/10.1016/j.tox.2024.153815

Filling the Blank Space: Branched 4-Nonylphenol Isomers Are Responsible for Robust Constitutive Androstane Receptor (CAR) Activation by Nonylphenol,
RASHIDIAN A., J. DUSEK, M. DRASTIK, L. SMUTNÁ, K. FRITSCHE, A. BRAEUNING, D. PIJNENBURG, R. VAN BEUNINGEN, P. HONKAKOSKI, A. POSO, T. KRONENBERGER and P. PAVEK, *Environmental Science & Technology* 58, no. 16 (Apr 2024): 6913-6923,
4-Nonylphenol (4-NP), a para-substituted phenolic compound with a straight or branched carbon chain, is a ubiquitous environmental pollutant and food contaminant. 4-NP, particularly the branched form, has been identified as an endocrine disruptor (ED) with potent activities on

estrogen receptors. Constitutive Androstane Receptor (CAR) is another crucial nuclear receptor that regulates hepatic lipid, glucose, and steroid metabolism and is involved in the ED mechanism of action. An NP mixture has been described as an extremely potent activator of both human and rodent CAR. However, detailed mechanistic aspects of CAR activation by 4-NP are enigmatic, and it is not known if 4-NP can directly interact with the CAR ligand binding domain (LBD). Here, we examined interactions of individual branched (22NP, 33NP, and 353NP) and linear 4-NPs with CAR variants using molecular dynamics (MD) simulations, cellular experiments with various CAR expression constructs, recombinant CAR LBD in a TR-FRET assay, or a differentiated HepaRG hepatocyte cellular model. Our results demonstrate that branched 4-NPs display more stable poses to activate both wild-type CAR1 and CAR3 variant LBDs in MD simulations. Consistently, branched 4-NPs activated CAR3 and CAR1 LBD more efficiently than linear 4-NP. Furthermore, in HepaRG cells, we observed that all 4-NPs upregulated CYP2B6 mRNA, a relevant hallmark for CAR activation. This is the first study to provide detailed insights into the direct interaction between individual 4-NPs and human CAR-LBD, as well as its dominant variant CAR3. The work could contribute to the safer use of individual 4-NPs in many areas of industry. https://doi.org/10.1021/acs.est.3c10096

Glyphosate presence in human sperm: First report and positive correlation with oxidative stress in an infertile French population,
VASSEUR C., L. SERRA, S. EL BALKHI, G. LEFORT, C. RAMÉ, P. FROMENT and J. DUPONT, *Ecotoxicol Environ Saf* 278 (Jun 15 2024): 116410,
Environmental exposure to endocrine disruptors, such as pesticides, could contribute to a decline of human fertility. Glyphosate (GLY) is the main component of Glyphosate Based Herbicides (GBHs), which are the most commonly herbicides used in the world. Various animal model studies demonstrated its reprotoxicity. In Europe, GLY authorization in agriculture has been extended until 2034. Meanwhile the toxicity of GLY in humans is still in debate. The aims of our study were firstly to analyse the concentration of GLY and its main metabolite, amino-methyl-phosphonic acid (AMPA) by LC/MS-MS in the seminal and blood plasma in an infertile French men population (n=128). We secondly determined Total Antioxidant Status (TAS) and Total Oxidant Status (TOS) using commercial colorimetric kits and some oxidative stress biomarkers including malondialdehyde (MDA) and 8-hydroxy-2'-deoxyguanosine (8-OHdG) by ELISA assays. We next analysed potential correlations between GLY and oxidative stress biomarkers concentration and sperm parameters (sperm concentration, progressive speed, anormal forms). Here, we detected for the first time GLY in the human seminal plasma in significant proportions and we showed that its concentration was four times higher than those observed in blood plasma. At the opposite, AMPA was undetectable. We also observed a strong positive correlation between plasma blood GLY concentrations and plasma seminal GLY and 8-OHdG concentrations, the latter reflecting DNA impact. In addition, TOS, Oxidative Stress Index (OSI) (TOS/TAS), MDA blood and seminal plasma concentrations were significantly higher in men with glyphosate in blood and seminal plasma, respectively. Taken together, our results suggest a negative impact of GLY on the human reproductive health and possibly on his progeny. A precaution principle should be applied at the time of the actual discussion of GLY and GBHs formulants uses in Europe by the authorities.
https://doi.org/10.1016/j.ecoenv.2024.116410

House dust-derived mixtures of organophosphate esters alter the phenotype, function, transcriptome, and lipidome of KGN human ovarian granulosa cells,
WANG X. T., A. ROWAN-CARROLL, M. J. MEIER, C. L. YAUK, M. G. WADE, B. ROBAIRE and B. F. HALES, *Toxicological Sciences* 200, no. 1 (May 2024): 95-113,
Organophosphate esters (OPEs), used as flame retardants and plasticizers, are present ubiquitously in the environment. Previous studies suggest that exposure to OPEs is detrimental to female fertility in humans. However, no experimental information is available on the effects of OPE

mixtures on ovarian granulosa cells, which play essential roles in female reproduction. We used high-content imaging to investigate the effects of environmentally relevant OPE mixtures on KGN human granulosa cell phenotypes. Perturbations to steroidogenesis were assessed using ELISA and qRT-PCR. A high-throughput transcriptomic approach, TempO-Seq, was used to identify transcriptional changes in a targeted panel of genes. Effects on lipid homeostasis were explored using a cholesterol assay and global lipidomic profiling. OPE mixtures altered multiple phenotypic features of KGN cells, with triaryl OPEs in the mixture showing higher potencies than other mixture components. The mixtures increased basal production of steroid hormones; this was mediated by significant changes in the expression of critical transcripts involved in steroidogenesis. Further, the total-OPE mixture disrupted cholesterol homeostasis and the composition of intracellular lipid droplets. Exposure to complex mixtures of OPEs, similar to those found in house dust, may adversely affect female reproductive health by altering a multitude of phenotypic and functional endpoints in granulosa cells. This study provides novel insights into the mechanisms of actions underlying the toxicity induced by OPEs and highlights the need to examine the effects of human relevant chemical mixtures. https://doi.org/10.1093/toxsci/kfae052

The Interplay between Endocrine-Disrupting Chemicals and the Epigenome towards Metabolic Dysfunction-Associated Steatotic Liver Disease: A Comprehensive Review,
NIKOLAOU E. M., I. P. KALAFATI and G. V. DEDOUSSIS, *Nutrients* 16, no. 8 (Apr 2024),
Metabolic dysfunction-associated steatotic liver disease (MASLD), described as the most prominent cause of chronic liver disease worldwide, has emerged as a significant public health issue, posing a considerable challenge for most countries. Endocrine-disrupting chemicals (EDCs), commonly found in daily use items and foods, are able to interfere with nuclear receptors (NRs) and disturb hormonal signaling and mitochondrial function, leading, among other metabolic disorders, to MASLD. EDCs have also been proposed to cause transgenerationally inherited alterations leading to increased disease susceptibility. In this review, we are focusing on the most prominent linking pathways between EDCs and MASLD, their role in the induction of epigenetic transgenerational inheritance of the disease as well as up-to-date practices aimed at reducing their impact.
https://doi.org/10.3390/nu16081124

The male reproductive toxicity after 5-Fluorouracil exposure: DNA damage, oxidative stress, and mitochondrial dysfunction in vitro and in vivo,
YUAN W. Z., G. J. JI, X. W. SHI, Z. B. SUN, C. Y. LIU, Y. Y. YU, W. M. LI, X. Y. WANG and H. H. HU, *Ecotoxicology and Environmental Safety* 278 (Jun 2024),
5-Fluorouracil (5-FU), a chemotherapeutic drug used to treat a variety of cancers, can enter the environment through different routes, causing serious public health and environmental concerns. It has been reported that 5FU exposure adversely affects male reproductive function, and its effects on this system cannot be avoided. In this study, using western blotting and quantitative polymerase chain reaction studies, we found that 5-FU promoted testicular injury by inducing oxidative stress, which was accompanied by the inhibition of nuclear factor erythroid 2-related factor 2/antioxidant response element signaling. Accumulation of reactive oxygen species (ROS) aggravated 5-FU-mediated mitochondrial dysfunction and apoptosis in murine cell lines and testes, indicating oxidative stress and mitochondrial-dependent apoptotic signaling play crucial roles in the damage of spermatogenic cells caused. N-Acetyl-L-cysteine, an antioxidant that scavenges intracellular ROS, protected spermatogenic cells from 5-FU-induced oxidative damage and mitochondrial dysfunction, revealing the important role of ROS in testicular dysfunction caused by 5-FU. We found that 5-FU exposure induces testicular cell apoptosis through ROS-mediated mitochondria pathway in mice. In summary, our findings revealed the reproductive toxicological effect of 5-FU on mice and its mechanism, provided basic data reference for adverse ecological and human health outcomes associated with 5-FU contamination or poisoning. https://doi.org/10.1016/j.ecoenv.2024.116465

Obesogenic effects of six classes of emerging contaminants,
WU S. Y., C. Y. TONG and J. LIU, *Journal of Environmental Sciences* 151 (May 2025): 252-272,
There is growing concern about the concept that exposure to environmental chemicals may be contributing to the obesity epidemic. However, there is no consensus on the obesogenic effects of emerging contaminants from a toxicological and environmental perspective. The potential human exposure and experimental evidence for obesogenic effects of emerging contaminants need to be systematically discussed. The main objective of this review is to provide recommendations for further subsequent policy development following a critical analysis of the literature for humans and experimental animals exposed to emerging contaminants. This article reviews human exposure to emerging contaminants (with a focus on antimicrobials, preservatives, water and oil repellents, flame retardants, antibiotics and bisphenols) and the impact of emerging contaminants on obesity. These emerging contaminants have been widely detected in human biological samples. Epidemiological studies provide evidence linking exposure to emerging contaminants to the risks of obesity in humans. Studies based on animal models and adipose cells show the obesogenic effects of emerging contaminants and identify modes of action by which contaminants may induce changes in body fat accumulation and lipid metabolic homeostasis. Some knowledge gaps in this area and future directions for further investigation are discussed. (c) 2024 The Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences. Published by Elsevier B.V. https://doi.org/10.1016/j.jes.2024.03.032

Paternal exposures to endocrine-disrupting chemicals induce intergenerational epigenetic influences on offspring: A review,
ZHANG Y. N., B. Y. WANG, W. H. SUN, G. H. WANG, Z. Q. LIU, X. F. ZHANG, J. F. DING, Y. HAN and H. J. ZHANG, *Environment International* 187 (May 2024),
Endocrine-disrupting chemicals (EDCs) are ubiquitous in ecological environments and have become a great issue of public health concern since the 1990 s. There is a deep scientific understanding of the toxicity of EDCs. However, recent studies have found that the abnormal physiological functions of the parents caused by EDCs could be transmitted to their unexposed offspring, leading to intergenerational toxicity. We questioned whether sustained epigenetic changes occur through the male germline. In this review, we (1) systematically searched the available research on the intergenerational impacts of EDCs in aquatic and mammal organisms, including 42 articles, (2) summarized the intergenerational genetic effects, such as decreased offspring survival, abnormal reproductive dysfunction, metabolic disorders, and behavioral abnormalities, (3) summarized the mechanisms of intergenerational toxicity through paternal interactions, and (4) propose suggestions on future research directions to develop a deeper understanding of the ecological risk of EDCs. https://doi.org/10.1016/j.envint.2024.108689

Per- and polyfluoroalkyl substances (PFAS) exposure in plasma and their blood-brain barrier transmission efficiency-A pilot study,
XIE M. Y., Z. Y. LIN, X. F. SUN, J. J. FENG, L. MAI, C. C. WU, G. L. HUANG, P. WANG, Y. W. LIU, L. Y. LIU and E. Y. ZENG, *Environ Int* 187 (May 2024): 108719,
Per- and polyfluoroalkyl substances (PFAS) have been shown to penetrate the blood-brain barrier (BBB) and accumulate in human brain. The BBB transmission and accumulation efficiency of PFAS, as well as the potential health risks from human co-exposure to legacy and emerging PFAS due to differences in transport efficiency, need to be further elucidated. In the present pilot study, 23 plasma samples from glioma patients were analyzed for 17 PFAS. The concentrations of PFAS in six paired brain tissue and plasma samples were used to calculate the BBB transmission efficiency of PFAS (R(PFAS)). This R(PFAS) analysis was conducted with utmost care and consideration amid the limited availability of valuable paired samples. The results indicated that low molecular weight

PFAS, including short-chain and emerging PFAS, may have a greater potential for accumulation in brain tissue than long-chain PFAS. As an alternative to perfluorooctane sulfonic acid (PFOS), 6:2 chlorinated polyfluorinated ether sulfonate (6:2 Cl-PFESA) exhibited brain accumulation potential similar to that of PFOS, suggesting it may not be a suitable substitute concerning health risk in brain. The BBB transmission efficiencies of perfluorooctanoic acid, PFOS, and 6:2 Cl-PFESA showed similar trends with age, which may be an important factor influencing the entry of exogenous compounds into the brain. A favorable link between perfluorooctane sulfonamide (FOSA) and the development and/or progression of glioma may be implicated by a strong positive correlation ($r(2) = 0.94$; $p < 0.01$) between R(FOSA) and Ki-67 (a molecular marker of glioma). However, a causal relationship between R(FOSA) and glioma incidence were not established in the present study. The present pilot study conducted the first examination of BBB transmission efficiency of PFAS from plasma to brain tissue and highlighted the importance of reducing and/or controlling exposure to PFAS. https://doi.org/10.1016/j.envint.2024.108719

Potential Adverse Outcome Pathways of Chlorinated Organophosphate Flame Retardants,
ZHOU M., H. ZHANG, Q. XIAO, K. LI, X. LI and H. CHU, *China CDC Wkly* 6, no. 23 (Jun 7 2024): 542-546,
WHAT IS ALREADY KNOWN ABOUT THIS TOPIC? Chlorinated organophosphate flame retardants (Cl-OPFRs) are frequently detected chemicals in the environment and biological samples, yet there is a lack of systematic evaluation regarding the adverse effects and toxicological mechanisms of Cl-OPFRs. WHAT IS ADDED BY THIS REPORT? This study utilizes the adverse outcome pathway (AOP) framework to assess the health implications and mechanisms of Cl-OPFRs, identifying multi-system toxicity, with a particular emphasis on reproductive issues and the possible toxic mechanisms. WHAT ARE THE IMPLICATIONS FOR PUBLIC HEALTH PRACTICE? These results enhance knowledge of the health hazards linked to Cl-OPFRs, supporting the creation of focused risk evaluations and suitable regulatory actions. https://doi.org/10.46234/ccdcw2024.105

Single and mixture effects of bisphenol A and benzophenone-3 on in vitro T helper cell differentiation,
FISCHER F., M. R. ERMER, J. HOWANSKI, Z. R. YIN, M. BAUER, M. WAGNER, B. FINK, A. C. ZENCLUSSEN and A. SCHUMACHER, *Chemico-Biological Interactions* 395 (May 2024),
Immune homeostasis is key to guarantee that the immune system can elicit effector functions against pathogens and at the same time raise tolerance towards other antigens. A disturbance of this delicate balance may underlie or at least trigger pathologies. Endocrine disrupting chemicals (EDCs) are increasingly recognized as risk factors for immune dysregulation. However, the immunotoxic potential of specific EDCs and their mixtures is still poorly understood. Thus, we aimed to investigate the effect of bisphenol A (BPA) and benzophenone-3 (BP-3), alone and in combination, on in vitro differentiation of T helper (TH)17 cells and regulatory T (Treg) cells. Na & iuml;ve T cells were isolated from mouse lymphoid tissues and differentiated into the respective TH population in the presence of 0.001-10 mu M BP-3 and/or 0.01-100 mu M BPA. Cell viability, proliferation and the expression of TH lineage specific transcription factors and cytokines was measured by flow cytometry and CBA/ELISA. Moreover, the transcription of hormone receptors as direct targets of EDCs was quantified by RT-PCR. We found that the highest BPA concentration adversely affected TH cell viability and proliferation. Moreover, the general differentiation potential of both TH populations was not altered in the presence of both EDCs. However, EDC exposure modulated the emergence of TH17 and Treg cell intermediate states. While BPA and BP-3 promoted the development of TH1-like TH17 cells under TH17-differentiating conditions, TH2-like Treg cells occurred under Treg polarization. Interestingly, differential effects could be observed in mixtures of the two tested compounds compared with the individual compounds. Notably, estrogen receptor beta expression was decreased under TH17-differentiating conditions in the

presence of BPA and BP-3 as mixture. In conclusion, our study provides solid evidence for both, the immune disruptive potential and the existence of cumulative effects of real nature EDC mixtures on T cell in vitro differentiation. https://doi.org/10.1016/j.cbi.2024.111011

Synthetic phenolic compounds perturb lipid metabolism and induce obesogenic effects,
LIU H. N., Z. D. SUN, Q. S. LIU, Q. F. ZHOU and G. B. JIANG, *Chinese Journal of Chromatography* 42, no. 2 (Feb 2024): 131-141,
Given continuous development in society and the economy, obesity has become a global epidemic, arousing great concern. In addition to genetic and dietary factors, exposure to environmental chemicals is associated with the occurrence and development of obesity. Current research has indicated that some chemicals with endocrine-disrupting effects can affect lipid metabolism in vivo, causing elevated lipid storage. These chemicals are called " environmental obesogens". Synthetic phenolic compounds (SPCs) are widely used in industrial and daily products, such as plastic products, disinfectants, pesticides, food additives, and so on. The exposure routes of SPCs to the human body may include food and water consumption, direct skin contact, etc. Their unintended exposure could cause harmful effects on human health. As a type of endocrine disruptor, SPCs interfere with adipogenesis and lipid metabolism, exhibiting the characteristics of environmental obesogens. Because SPCs have similar phenolic structures, gathering information on their influences on lipid metabolism would be helpful to understand their structure-related effects. In this review, three commonly used research methods for screening environmental obesogens, including in vitro testing for molecular interactions, cell adipogenic differentiation models, and in vivo studies on lipid metabolism, are summarized, and the advantages and disadvantages of these methods are compared and discussed. Based on both in vitro and in vivo data, three types of SPCs, including bisphenol A (BPA) and its ana. logues, alkylphenols (APs), and synthetic phenolic antioxidants (SPAs), are systematically discussed in terms of their ability to disrupt adipogenesis and lipid metabolism by focusing on adipose and hepatic tissues, among others. Common findings on the effects of these SPCs on adipocyte differentiation, lipid storage, hepatic lipid accumulation, and liver steatosis are de. scribed. The underlying toxicological mechanisms are also discussed from the aspects of nuclear receptor transactivation, inflammation and oxidative stress regulation, intestinal microenvi. ronment alteration, epigenetic modification, and some other signaling pathways. Future research to increase public knowledge on the obesogenic effects of emerging chemicals of concern is encouraged. https://doi.org/10.3724/sp.J.1123.2023.12018

A System Biology Approach Reveals New Targets for Human Thyroid Gland Toxicity in Embryos and Adult Individuals,
OLIVEIRA J. M., J. ZENZELUK, C. SERRANO-NASCIMENTO, M. A. ROMANO and R. M. ROMANO, *Metabolites* 14, no. 4 (Apr 2024),
Compounds of natural or synthetic origin present in personal care products, food additives, and packaging may interfere with hormonal regulation and are called endocrine-disrupting chemicals (EDCs). The thyroid gland is an important target of these compounds. The objective of this study was to analyze public data on the human thyroid transcriptome and investigate potential new targets of EDCs in the embryonic and adult thyroid glands. We compared the public transcriptome data of adult and embryonic human thyroid glands and selected 100 up- or downregulated genes that were subsequently subjected to functional enrichment analysis. In the embryonic thyroid, the most highly expressed gene was PRMT6, which methylates arginine-4 of histone H2A (86.21%), and the downregulated clusters included plasma lipoprotein particles (39.24%) and endopeptidase inhibitory activity (24.05%). For the adult thyroid gland, the most highly expressed genes were related to the following categories: metallothionein-binding metals (56.67%), steroid hormone biosynthetic process (16.67%), and cellular response to vascular endothelial growth factor stimulus (6.67%). Several compounds ranging from antihypertensive drugs to enzyme inhibitors were

identified as potentially harmful to thyroid gland development and adult function. https://doi.org/10.3390/metabo14040226

Triclocarban and triclosan promote breast cancer progression in vitro and in vivo via activating G protein-coupled estrogen receptor signaling pathways,
HE T. T., X. LI, J. Z. MA, Y. YANG, S. Y. ZHU, J. H. ZENG, L. LUO, Y. L. YIN and L. Y. CAO, *Science of the Total Environment* 931 (Jun 2024),
Triclocarban (TCC) and triclosan (TCS) have been detected ubiquitously in human body and evoked increasing concerns. This study aimed to reveal the induction risks of TCC and TCS on triple negative breast cancer through non-genomic GPER-mediated signaling pathways. Molecular simulation indicated that TCC exhibited higher GPER binding affinity than TCS theoretically. Calcium mobilization assay displayed that TCC/TCS activated GPER signaling pathway with the lowest observed effective concentrations (LOEC) of 10 nM/100 nM. TCC and TCS also upregulated MMP-2/9, EGFR, MAPK3 but downregulated MAPK8 via GPER-mediated signaling pathway. Proliferation assay showed that TCC/TCS induced 4 T1 breast cancer cells proliferation with the LOEC of 100 nM/1000 nM. Wound-healing and transwell assays showed that TCC/TCS promoted 4 T1 cells migration in a concentration-dependent manner with the LOEC of 10 nM. The effects of TCC on breast cancer cells proliferation and migration were stronger than TCS and both were regulated by GPER. TCC/TCS induced migratory effects were more significantly than proliferative effect. Mechanism study showed that TCC/TCS downregulated the expression of epithelial marker (E-cadherin) but upregulated mesenchymal markers (snail and N-cadherin), which was reversed by GPER inhibitor G15. These biomarkers results indicated that TCC/TCS-induced 4 T1 cells migration was a classic epithelial to mesenchymal transition mechanism regulated by GPER signaling pathway. Orthotopic tumor model verified that TCC promoted breast cancer in-situ tumor growth and distal tissue metastasis via GPER-mediated signaling pathway at human-exposure level of 10 mg/kg/d. TCC-induced tissue metastasis of breast cancer was more significantly than in-situ tumor growth. Overall, we demonstrated for the first time that TCC/TCS could activate the GPER signaling pathways to induce breast cancer progression. https://doi.org/10.1016/j.scitotenv.2024.172782

Evaluation de l'exposition

Beyond the Tailpipe: An Outdated Flammability Standard Leads to Organohalogen Flame Retardant Exposures inside Cars,
BIRNBAUM L. S. and J. M. FLEMING, *Environ Sci Technol* 58, no. 23 (Jun 11 2024): 9909-9911, https://doi.org/10.1021/acs.est.4c03540

Ongoing exposure to endocrine disrupting phthalates and alternative plasticizers in neonatal intensive care unit patients,
PANNEEL L., P. CLEYS, G. POMA, Y. A. BAMAI, P. G. JORENS, A. COVACI and A. MULDER, *Environment International* 186 (Apr 2024),
Due to endocrine disrupting effects, di-(2-ethylhexyl) phthalate (DEHP), a plasticizer used to soften plastic medical devices, was restricted in the EU Medical Devices Regulation (EU MDR 2017/745) and gradually replaced by alternative plasticizers. Neonates hospitalized in the neonatal intensive care unit (NICU) are vulnerable to toxic effects of plasticizers. From June 2020 to August 2022, urine samples (n = 1070) were repeatedly collected from premature neonates (n = 132, 4-10 samples per patient) born at <31 weeks gestational age and/or <1500 g birth weight in the Antwerp University

Hospital, Belgium. Term control neonates (n = 21, 1 sample per patient) were included from the maternity ward. Phthalate and alternative plasticizers' metabolites were analyzed using liquid-chromatography coupled to tandem mass spectrometry. Phthalate metabolites were detected in almost all urine samples. Metabolites of alternative plasticizers, di-(2-ethylhexyl)-adipate (DEHA), di(2-ethylhexyl)-terephthalate (DEHT) and cyclohexane-1,2-dicarboxylic-di-isononyl-ester (DINCH), had detection frequencies ranging 30-95 %. Urinary phthalate metabolite concentrations were significantly higher in premature compared to control neonates (p = 0.023). NICU exposure to respiratory support devices and blood products showed increased phthalate metabolite concentrations (p < 0.001). Phthalate exposure increased from birth until four weeks postnatally. The estimated phthalate intake exceeded animal-derived no-effect-levels (DNEL) in 10 % of samples, with maximum values reaching 24 times the DNEL. 29 % of premature neonates had at least once an estimated phthalate intake above the DNEL. Preterm neonates are still exposed to phthalates during NICU stay, despite the EU Medical Devices Regulation. NICU exposure to alternative plasticizers is increasing, though currently not regulated, with insufficient knowledge on their hazard profile. https://doi.org/10.1016/j.envint.2024.108605

Prevalence of synthetic phenolic antioxidants in food contact materials from China and their implications for human dietary exposure through take-away food,
HAN B., Y. Z. SHANG, H. WANG, Y. SHEN, R. F. LI, M. Y. WANG, Z. J. ZHUANG, Z. WANG, M. FANG and T. JING, *Journal of Hazardous Materials* 473 (Jul 2024),
The application of disposable tableware has increased substantially in recent times due to the rapidly growing food delivery business in China. Synthetic phenolic antioxidants (SPAs) are widely used in food contact materials (FCMs) to delay the process of oxidation; however, their compositions, concentrations, and potential health hazards remain unclear. Therefore, FCMs comprised of five materials obtained from 19 categories (n = 118) in China were analyzed for SPAs concentrations. FCMs have been found to contain a variety of SPAs, with & sum;SPAs concentrations ranging from 44.18 to 69,485.12 mu g/kg (median: 2615.63 mu g/kg). The predominant congeners identified in the sample include 2,4-di-tert-butylphenol (2,4-DTBP), 2,6-di-tert-butylphenol (2,6-DTBP), and 2,6di-tert-butyl-p-benzoquinone (BHT -Q) with a median concentration of 885.75, 555.45 and of 217.44 mu g/kg, respectively. Milky tea paper cups, instant noodle buckets, milky teacups, and disposable cups showed high levels of SPAs. 2,2 ' -methylenebis(4-methyl-6-tert-butylphenol) (AO 2246) was predominantly detected in polyethylene and polyethylene terephthalate-based products. The migration test identified disposable plastic cups and bowls as the predominant FCMs and 2,4-DTBP as the dominant SPA. The exposure risk of Sigma SPAs decreased with age. In children, the estimated daily intake of & sum;SPAs from FCMs was determined to be 17.56 ng/kg body weight/day, which was 8.3 times higher than that of phthalic acid esters. The current findings indicate the potential ingestion risk of SPAs during the daily life application of multiple FCM categories. https://doi.org/10.1016/j.jhazmat.2024.134599

Thèse - Evaluation de l'exposition des enfants de moins de 36 mois aux phtalates (di-2-ethylhexyl phthalate (DEHP) et di-iso-nonyl phthalate (DINP)) via les jouets en plastique type polychlorure de vinyle souple (PVC) commercialisés dans la région du Nord Algérien,
A Y., *Setif Universite Ferhat Abbas faculté de médecine* (2024),
Les enfants âgés de moins de 36 mois, constituent une population spécifique, particulièrement vulnérable aux risques toxiques liés aux phtalates. L'objectif principal de cette étude était d'évaluer les niveaux d'exposition des enfants de moins de 3 mois au DEHP et au DINP via les jouets en PVC neufs commercialisés dans la région du Nord algérien (Sétif, Constantine, Annaba, Bejaia, Alger et Oran). L'étude visait également à évaluer les niveaux de ces phtalates dans ces jouets. Il s'agit d'une étude transversale expérimentale qui s'est portée sur 271 jouets en plastique souple. La fréquence relative des jouets en PVC souple était estimée à 55%. Le DEHP était plus fréquemment quantifié

dans les jouets en PVC par rapport au DINP. Notre étude a mis en évidence des concentrations de DEHP et de DINP très variables. La concentration moyenne de DEHP était de 7,63 ± 9,80%, et la concentration moyenne de DINP s'établissait à 4,69 ± 10,14%. Nous avons conclu que 75,2% des jouets en PVC analysés, étaient non conformes par rapport à leur teneur en phtalates (DEHP et/ou DINP). Le DEHP était l'origine de la non-conformité de 65,8% des jouets en PVC. Le pourcentage massique le plus élevé de DEHP était plus de 362 fois supérieure à la limite autorisée dans de nombreux pays (0,1%). La concentration de DINP dépassait cette limite dans 29,5% des jouets en PVC. Le pourcentage massique le plus élevé était plus de 354 fois supérieure à la limite autorisée. Le taux de migration moyen de DEHP et de DINP in vitro était de 1,54 ± 0,92µg/10cm2/min et de 1,90 ± 1,34µg/10cm2/min respectivement.13 jouets ont donné un taux de migration supérieur à la valeur guide fixée, et aucune jouet n'a donné un taux de migration de DINP supérieur à la valeur guide. Nous avons constaté une forte corrélation, statistiquement significative, entre le taux de migration in vitro du DEHP et la teneur des jouets en DEHP (p/p). Cependant, nous avons observé une corrélation moyenne, statistiquement non significative, entre vle taux de migration de DINP in vitro et la teneur du jouet en DINP (p/p). vLe taux moyen de migration in vivo de DEHP et de DINP était de 0,68 ± v0,33µg/10cm2/min, et de 0,97 ± 0,40µg/10cm2/min respectivement. Comme dans le test dev migration salivaire in vitro, la migration in vivo n'a été observée que pour les teneurs élevées en phtalates. Nous avons constaté une faible corrélation, statistiquement non significative, entre le taux de migration de DEHP in vivo et la teneur en DEHP (p/p). La corrélation entre la teneur de jouet en DINP et la migration vers la salive des adultes volontaires était statistiquement non significative également. Nous avons constaté une corrélation moyenne, statistiquement non significative, entre le taux de migration de DEHP in vitro et in vivo. La corrélation entre le taux de migration de DINP in vitro et in vivo a montré une faible corrélation, statistiquement non significative. La DJE de ces deux phtalates chez les enfants moins de 36 mois était significativement inférieure à la dose journalière tolérable. Notre étude a permi de conclure que l'exposition isolée au DINP ou au DEHP, lors de la mise en bouche de jouets en plastique souple n'est pas susceptible de présenter un risque pour la santé des enfants moins de 36 mois dans le contexte d'une exposition chronique (HI < 1). https://catalogue-biblio.univ-setif.dz/opac/index.php?lvl=notice_display&id=133121

Widespread occurrence of pesticides in low-income housing,
VAEZAFSHAR S., J. A. SIEGEL, L. JANTUNEN and M. L. DIAMOND, *Journal of Exposure Science and Environmental Epidemiology* (2024 Jun 2024),
Background Low socioeconomic status (SES) residents living in social housing, which is subsidized by government or government-funded agencies, may have higher exposures to pesticides used in indoor residences since pesticides are applied due to structural deficiencies, poor maintenance, etc.Objective To estimate exposure of residents in low-SES social housing built in the 1970s to legacy and current-use pesticides and to investigate factors related to exposures.Methods Twenty-eight particle-phase pesticides were measured in the indoor air of 46 units in seven low-income social housing, multi-unit residential buildings (MURBs) in Toronto, Canada using portable air cleaners deployed for 1 week in 2017. Pesticides analyzed were legacy and current use in the classes: organochlorines, organophosphates, pyrethroids, and strobilurins.Results At least one pesticide was detected in 89% of the units with detection frequencies (DF) for individual pesticides of up to 50%, including legacy organochlorines and current-use pesticides. Current-use pyrethroids had the highest DF and concentrations, with the highest particle-phase concentration for pyrethrin I at 32,000 pg/m3. Heptachlor, restricted for use in Canada in 1985, had the highest estimated maximum total air (particle plus gas phase) concentration of 443,000 pg/m3. Heptachlor, lindane, endosulfan I, chlorothalonil, allethrin, and permethrin (except in one study) had higher concentrations than those measured in low-income residences reported elsewhere. In addition to

the intentional use of pesticides to control pests and their use in building materials and paints, tobacco smoking was significantly correlated with the concentrations of five pesticides used on tobacco crops. The distribution of pesticides with high DF in individual buildings suggested that pest eradication programs by the building management and/or pesticide use by residents were the major sources of measured pesticides.Impact Low-income social housing fills a much-needed demand, but the residences are prone to pest infestation and hence pesticide use. We found exposure to at least 1 of 28 particle-phase pesticides in 89% of all 46 units tested, with the highest DF and concentrations for current-use pyrethroids and long-banned organochlorines (e.g., DDT, heptachlor) due to very high persistence indoors. Also measured were several pesticides not registered for use indoors, e.g., strobilurins used to treat building materials and pesticides used on tobacco crops. These results, which are the first Canadian data for most pesticides indoors, show widespread exposure to numerous pesticides. https://doi.org/10.1038/s41370-024-00665-y

Méthodes

Advancing toxicity studies of per- and poly-fluoroalkyl substances (pfass) through machine learning: Models, mechanisms, and future directions,
MENG L., B. ZHOU, H. LIU, Y. CHEN, R. YUAN, Z. CHEN, S. LUO and H. CHEN, *Sci Total Environ* 946 (Jun 25 2024): 174201,
Perfluorinated and perfluoroalkyl substances (PFASs), encompassing a vast array of isomeric chemicals, are recognized as typical emerging contaminants with direct or potential impacts on human health and the ecological environment. With the complex and elusive toxicological profiles of PFASs, machine learning (ML) has been increasingly employed in their toxicity studies due to its proficiency in prediction and data analytics. This integration is poised to become a predominant trend in environmental toxicology, propelled by the swift advancements in computational technology. This review diligently examines the literature to encapsulate the varied objectives of employing ML in the toxicity studies of PFASs: (1) Utilizing ML to establish Quantitative Structure-Activity Relationship (QSAR) models for PFASs with diverse toxicity endpoints, facilitating the targeted toxicity prediction of unidentified PFASs; (2) Investigating and substantiating the Adverse Outcome Pathway (AOP) through the synergy of ML and traditional toxicological methods, with this refining the toxicity assessment framework for PFASs; (3) Dissecting and elucidating the features of established ML models to advance Open Research into the toxicity of PFASs, with a primary focus on determinants and mechanisms. The discourse extends to an in-depth examination of ML studies, segregating findings based on their distinct application trajectories. Given that ML represents a nascent paradigm within PFASs research, this review delineates the collective challenges encountered in the ML-mediated study of PFAS toxicity and proffers strategic guidance for ensuing investigations. https://doi.org/10.1016/j.scitotenv.2024.174201

Bisphenol A and its analogues: from their occurrence in foodstuffs marketed in Europe to improved monitoring strategies-a review of published literature from 2018 to 2023,
NERI I., G. RUSSO and L. GRUMETTO, *Archives of Toxicology* (2024 Jun 2024),
In this review article, the research works covering the analytical determination of bisphenol A (BPA) and its structural analogues published from 2018 to present (February 2024) were examined. The review offers an overview of the concentration levels of these xenoestrogens in food and beverages, and discusses concerns that these may possibly pose to the human health and scrutinises, from an analytical perspective, the main biomonitoring approaches that are applied. This comes as a natural evolution of a previous review that covered the same topic but in earlier

years (up to 2017). As compared to the past, while the volume of published literature on this topic has not necessarily decreased, the research studies are now much more homogeneous in terms of their geographical origin, i.e., Southern Europe (mainly Italy and Spain). For this reason, an estimated daily intake of the European population could not be calculated at this time. In terms of the analytical approaches that were applied, 67% of the research groups exploited liquid chromatography (LC), with a detection that was prevalently (71%) afforded by mass spectrometry, with over one-fourth of the research teams using fluorescence (26%) and a minority (3%) detecting the analytes with diode array detection. One-third of the groups used gas chromatography (GC)-mass spectrometry achieving comparatively superior efficiency as compared to LC. Derivatisation was performed in 59% of the GC studies to afford more symmetrical signals and enhanced sensitivity. Although the contamination levels are well below the threshold set by governments, routinely biomonitoring is encouraged because of the possible accumulation of these contaminants in the human body and of their interplay with other xenoestrogens.
https://doi.org/10.1007/s00204-024-03793-4

Electro-assisted liquid phase microextraction for the determination of parabens and their main metabolites in maternal urine and amniotic fluid samples,
LEO-MARTOS E., N. ARANDA-MERINO, R. SANCHEZ-RUIZ, I. M. MORENO, R. FERNÁNDEZ-TORRES and M. RAMOS-PAYÁN, *Microchemical Journal* 200 (May 2024),
In this study, an electro assisted liquid phase microextraction (EA-LPME) procedure to determine seven parabens (methyl, ethyl, propyl, isopropyl, butyl, isobutyl, and benzyl paraben) and three of their key hydroxy metabolites (4-hydroxy, 3,4-dihydroxy, and 3,4,5-trihydroxy benzoic acid) was optimised in maternal urine and amniotic fluid obtained at delivery from pregnant women. The samples were analysed by ultra-high-performance liquid chromatography coupled with electrospray ionisation tandem mass spectrometry (UPLC-ESI-MS/MS). PHBs and their metabolites were extracted from a pH 4 donor solution (10 mL) into a pH 13 acceptor solution (50 mu L) using 1-octanol as the supported liquid membrane (SLM) and 30 V for 40 min at 400 rpm. Under optimal operational conditions, enrichment factors between 10 and 90 were achieved, and low quantitation limits within 0.022-0.20ng mL-1 and 0.025-0.18 ng mL-1, were obtained for amniotic fluid and urine, respectively. The proposed analytical procedure was satisfactorily applied for the determination of target compounds in seven paired maternal urine and amniotic fluid samples to evaluate the possible placental transfer of these compounds from mothers to babies.
https://doi.org/10.1016/j.microc.2024.110321

Enhanced identification of endocrine disruptors through integration of science-based regulatory practices and innovative methodologies: The MERLON Project,
SVINGEN T., A. M. ANDERSSON, J. ANGELOVA, M. AXELSTAD, J. BAKKER, L. BAUMANN, A. BERONIUS, N. BOUFTAS, F. CHALMEL, S. CHRISTIANSEN, C. CORNIL, P. DAMDIMOPOULOU, D. DEEPIKA, M. E. T. DOLLÉ, M. K. DRASKAU, M. B. FISCHER, C. P. HAGEN, E. HESSEL, M. L. HOLMER, S. HUGHES, G. JENSEN, H. K. L. JOHANSSON, A. JUUL, V. KUMAR, S. KUMAR, A. LARDENOIS, K. M. MAIN, S. MAZAUD-GUITTOT, S. J. MOE, G. MOLA, A. S. PARENT, R. PINEDA, A. ROLLAND, A. K. ROSENMAI, Y. SONG, A. SUGLIA, M. TENA-SEMPERE, L. WEHRLI, J. ZILLIACUS and M. VAN DUURSEN, *Open Res Eur* 4 (2024): 68,
The prevalence of hormone-related health issues caused by exposure to endocrine disrupting chemicals (EDCs) is a significant, and increasing, societal challenge. Declining fertility rates together with rising incidence rates of reproductive disorders and other endocrine-related diseases underscores the urgency in taking more action. Addressing the growing threat of EDCs in our environment demands robust and reliable test methods to assess a broad variety of endpoints relevant for endocrine disruption. EDCs also require effective regulatory frameworks, especially as the current move towards greater reliance on non-animal methods in chemical testing puts to test

the current paradigm for EDC identification, which requires that an adverse effect is observed in an intact organism. Although great advances have been made in the field of predictive toxicology, disruption to the endocrine system and subsequent adverse health effects may prove particularly difficult to predict without traditional animal models. The MERLON project seeks to expedite progress by integrating multispecies molecular research, new approach methodologies (NAMs), human clinical epidemiology, and systems biology to furnish mechanistic insights and explore ways forward for NAM-based identification of EDCs. The focus is on sexual development and function, from foetal sex differentiation of the reproductive system through mini-puberty and puberty to sexual maturity. The project aims are geared towards closing existing knowledge gaps in understanding the effects of EDCs on human health to ultimately support effective regulation of EDCs in the European Union and beyond. https://doi.org/10.12688/openreseurope.17319.1

Estimating the dynamic early life exposure to PFOA and PFOS of the HELIX children: Emerging profiles via prenatal exposure, breastfeeding, and diet,
RATIER A., M. CASAS, R. GRAZULEVICIENE, R. SLAMA, L. SMÅSTUEN HAUG, C. THOMSEN, M. VAFEIADI, J. WRIGHT, F. A. ZEMAN, M. VRIJHEID and C. BROCHOT, *Environment International* 186 (2024/04/01/ 2024): 108621,
In utero and children's exposure to per- and polyfluoroalkyl substances (PFAS) is a major concern in health risk assessment as early life exposures are suspected to induce adverse health effects. Our work aims to estimate children's exposure (from birth to 12 years old) to PFOA and PFOS, using a Physiologically-Based Pharmacokinetic (PBPK) modelling approach. A model for PFAS was updated to simulate the internal PFAS exposures during the in utero life and childhood, and including individual characteristics and exposure scenarios (e.g., duration of breastfeeding, weight at birth, etc.). Our approach was applied to the HELIX cohort, involving 1,239 mother–child pairs with measured PFOA and PFOS plasma concentrations at two sampling times: maternal and child plasma concentrations (6 to 12 y.o). Our model predicted an increase in plasma concentrations during fetal development and childhood until 2 y.o when the maximum concentrations were reached. Higher plasma concentrations of PFOA than PFOS were predicted until 2 y.o, and then PFOS concentrations gradually became higher than PFOA concentrations. From 2 to 8 y.o, mean concentrations decreased from 3.1 to 1.88 µg/L or ng/mL (PFOA) and from 4.77 to 3.56 µg/L (PFOS). The concentration–time profiles vary with the age and were mostly influenced by in utero exposure (on the first 4 months after birth), breastfeeding (from 5 months to 2 (PFOA) or 5 (PFOS) y.o of the children), and food intake (after 3 (PFOA) or 6 (PFOS) y.o of the children). Similar measured biomarker levels can correspond to large differences in the simulated internal exposures, highlighting the importance to investigate the children's exposure over the early life to improve exposure classification. Our approach demonstrates the possibility to simulate individual internal exposures using PBPK models when measured biomarkers are scarce, helping risk assessors in gaining insight into internal exposure during critical windows, such as early life.
https://doi.org/10.1016/j.envint.2024.108621

Human biomonitoring of novel brominated flame retardants: A review on invasive and non-invasive biomarkers,
OLAGOKE O. M., T. O. OLUSEYI, K. L. NJOKU, S. HARRAD and M. A. ABDALLAH, *Emerging Contaminants* 10, no. 3 (Sep 2024),
Novel brominated flame retardants (NBFRs) are a group of chemicals applied mainly as alternatives to the phased-out polybrominated diphenyl ethers (PBDEs). However, toxicological studies show that NBFRs may pose health risks similar to PBDEs.The present study reviews available information on the biomonitoring of NBFRs and their metabolites in humans through invasive and non-invasive biomarkers, as well as the toxicological effects of these chemicals both in vivo and in vitro. In general, higher concentrations of NBFRs were reported in tissues of occupationally exposed adults

from NBFR production facilities, e-waste recycling facilities and inhabitants living close to these areas, compared to the general population. It is worth noting that NBFR human biomonitoring data are limited to few countries located in North America, Europe and Asia, while data from developing countries are scarce. Evidence from in vivo and in vitro toxicity studies show that several NBFRs can cause adverse health effects through various modes of action, mainly: hormone disruption, genotoxicity, endocrine disruption, and behavioural changes. Although few studies have investigated the biotransformation of NBFRs in humans, evidence suggests that the toxicity of some NBFRs may be augmented through their metabolites, as in the case of 2,3,4,5- tetrabromobenzoic acid (TBBA), which may exhibit higher toxicity than its parent compound 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (EH-TBB). More research is required to assess toxicity thresholds, toxic endpoints, and tolerable intakes for various NBFRs, and their metabolites in human. Comprehensive epidemiological studies are highly recommended to further understand the risk arising from human exposure to different NBFRs, particularly in occupational settings. https://doi.org/10.1016/j.emcon.2024.100378

Identification of endocrine-disrupting chemicals targeting key DCM-associated genes via bioinformatics and machine learning,
LI S., S. C. LIU, X. F. SUN, L. Y. HAO and Q. H. GAO, *Ecotoxicology and Environmental Safety* 274 (Apr 2024),
Dilated cardiomyopathy (DCM) is a primary cause of heart failure (HF), with the incidence of HF increasing consistently in recent years. DCM pathogenesis involves a combination of inherited predisposition and environmental factors. Endocrine-disrupting chemicals (EDCs) are exogenous chemicals that interfere with endogenous hormone action and are capable of targeting various organs, including the heart. However, the impact of these disruptors on heart disease through their effects on genes remains underexplored. In this study, we aimed to explore key DCM-related genes using machine learning (ML) and the construction of a predictive model. Using the Gene Expression Omnibus (GEO) database, we screened differentially expressed genes (DEGs) and performed enrichment analyses of Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways related to DCM. Through ML techniques combining maximum relevance minimum redundancy (mRMR) and least absolute shrinkage and selection operator (LASSO) logistic regression, we identified key genes for predicting DCM (IL1RL1, SEZ6L, SFRP4, COL22A1, RNASE2, HB). Based on these key genes, 79 EDCs with the potential to affect DCM were identified, among which 4 (3,4-dichloroaniline, fenitrothion, pyrene, and isoproturon) have not been previously associated with DCM. These findings establish a novel relationship between the EDCs mediated by key genes and the development of DCM. https://doi.org/10.1016/j.ecoenv.2024.116168

An in vitro model system for testing chemical effects on microbiome-immune interactions - examples with BPX and PFAS mixtures,
FISCHER F., A. PIERZCHALSKI, S. RIESBECK, A. S. ALDEHOFF, V. A. CASTANEDA-MONSALVE, S. B. HAANGE, M. VON BERGEN, U. E. ROLLE-KAMPCZYK, N. JEHMLICH, A. C. ZENCLUSSEN and G. HERBERTH, *Front Immunol* 15 (2024): 1298971,
INTRODUCTION: More than 350,000 chemicals make up the chemical universe that surrounds us every day. The impact of this vast array of compounds on our health is still poorly understood. Manufacturers are required to carry out toxicological studies, for example on the reproductive or nervous systems, before putting a new substance on the market. However, toxicological safety does not exclude effects resulting from chronic exposure to low doses or effects on other potentially affected organ systems. This is the case for the microbiome-immune interaction, which is not yet included in any safety studies. METHODS: A high-throughput in vitro model was used to elucidate the potential effects of environmental chemicals and chemical mixtures on microbiome-immune interactions. Therefore, a simplified human intestinal microbiota (SIHUMIx) consisting of

eight bacterial species was cultured in vitro in a bioreactor that partially mimics intestinal conditions. The bacteria were continuously exposed to mixtures of representative and widely distributed environmental chemicals, i.e. bisphenols (BPX) and/or per- and polyfluoroalkyl substances (PFAS) at concentrations of 22 µM and 4 µM, respectively. Furthermore, changes in the immunostimulatory potential of exposed microbes were investigated using a co-culture system with human peripheral blood mononuclear cells (PBMCs). RESULTS: The exposure to BPX, PFAS or their mixture did not influence the community structure and the riboflavin production of SIHUMIx in vitro. However, it altered the potential of the consortium to stimulate human immune cells: in particular, activation of CD8(+) MAIT cells was affected by the exposure to BPX- and PFAS mixtures-treated bacteria. DISCUSSION: The present study provides a model to investigate how environmental chemicals can indirectly affect immune cells via exposed microbes. It contributes to the much-needed knowledge on the effects of EDCs on an organ system that has been little explored in this context, especially from the perspective of cumulative exposure. https://doi.org/10.3389/fimmu.2024.1298971

An Integrated Approach of Bioassays and Non-Target Screening for the Assessment of Endocrine-Disrupting Activities in Tap Water and Identification of Novel Endocrine-Disrupting Chemicals, LIU S. Y. and J. LIU, *Toxics* 12, no. 4 (Apr 2024),
The safety of drinking water is a significant environmental issue of great concern for human health since numerous contaminants are often detected in drinking water and its sources. Boiling is a common household method used to produce relatively high-quality drinking water in some countries and regions. In this study, with the aid of an integrated approach of in vitro bioassays and non-target analysis based on high-resolution mass spectrometry coupled with liquid chromatography, alterations in endocrine-disrupting activities in tap water samples without and with boiling were revealed, as well as the potential endocrine-disrupting chemicals (EDCs) contributing to these alterations were identified. The organic extracts of tap water had no significant (ant)agonistic activities against an estrogen receptor (ER), progesterone receptor (PR), glucocorticoid receptor (GR), and mineralocorticoid receptor (MR) at enrichment concentrations of <= 10 times, posing no immediate or acute health risk to humans. However, the presence of agonistic activities against PR and MR and antagonistic activities against ER, PR, GR, and MR in OEs of tap water at relatively higher enrichment concentrations still raise potential health concerns. Boiling effectively reduced antagonistic activities against these steroid hormone receptors (SHRs) but increased estrogenic and glucocorticoid activities in drinking water. Four novel potential EDCs, including one UV filter (phenylbenzimidazole sulfonic acid, PBSA) and three natural metabolites of organisms (beta-hydroxymyristic acid, 12-hydroxyoctadecanoic acid, and isorosmanol) were identified in drinking water samples, each of which showed (ant)agonistic activities against different SHRs. Given the widespread use of UV filters in sunscreens to prevent skin cancer, the health risks posed by PBSA as an identified novel EDC are of concern. Although boiling has been thought to reduce the health risk of drinking water contamination, our findings suggest that boiling may have a more complex effect on the endocrine-disrupting activities of drinking water and, therefore, a more comprehensive assessment is needed. https://doi.org/10.3390/toxics12040247

Magnetic covalent organic frameworks combined with HPLC for determination of alkylphenols, CHENG T., Y. X. CHEN, Z. Y. LI, J. H. ZHU, J. ZHAO, Y. S. LIU and L. L. WANG, *Talanta Open* 9 (Aug 2024),
Alkylphenols are widely applied in the field of industry and agriculture, but their endocrine disrupting properties harm to human health. Moreover, alkylphenols often exhibit the low content in complex samples. Thus, we proposed magnetic covalent organic framework composites (Fe3O4@TatTpa) for efficient magnetic solid phase extraction (MSPE) of alkylphenols via hydrogen bonding, pi-pi and hydrophobic interactions. In combination with HPLC detection, good linearity

(0.006-10 mu g mL-1) with R2 (>= 0.997) and low limit of detections (1.8-6 x 10-3 mu g mL-1) were realized for alkylphenols. The proposed method was successfully employed to determine alkylphenols in soft drink, black oolong tea, and watermelon samples with satisfactory recoveries (86.1-118.5 %) and relative standard deviations (6.3-14.8 %).
https://doi.org/10.1016/j.talo.2024.100320

Optimization of a modified Captiva EMR-lipid method based on micro-matrix solid-phase dispersion coupled with gas chromatography-mass spectrometry for the determination of nine bisphenols in mussel samples,
CARRO N., R. FERNÁNDEZ, J. COBAS, I. GARCÍA, M. IGNACIO and A. MOUTEIRA, *Analytical Methods* 16, no. 24 (Jun 2024): 3957-3967,
This work describes a reliable, cheap, easy and fast method for analysis of nine bisphenols in mussel samples by gas chromatography-mass spectrometry after trimethylsilylation. The modified method consisted of miniaturized matrix solid phase dispersion (micro-MSPD) in a glass Pasteur pipette using Captiva EMR (enhanced matrix removal)-lipid as the sorbent. Good linearity was obtained in the work range (1-500 mu g L-1) with a correlation coefficient (R2) >= 0.998. The method accuracy and precision were determined at two concentration levels. The results show recoveries ranging from 55 to 111%. The precision varied from 1.95 to 11.4% (RSD). The whole quantification limits were between 0.056 and 3.42 mu g per kg dry weight. The analytical procedure was applied for the analyses of five mussel samples collected from Galician Rias. The major compound was BPA, and wild mussels from R & iacute;as de Ferrol, Vigo and A Coru & ntilde;a had the highest levels. The proposed method is suitable for the analysis of BPA and its analogues in mussel samples. This work describes a reliable, cheap, easy and fast method for analysis of nine bisphenols in mussel samples by gas chromatography-mass spectrometry after trimethylsilylation.
https://doi.org/10.1039/d4ay00738g

Actualité, Politique, Institutions et organismes scientifiques, Comptes rendus d'évènements, Evaluation du caractère PE des substances

ED Liste - List Update *Endocrine Disruptor Lists* (juin 2024),
List I
Propiconazole added since the ED proposal has now been legally adopted
Cyanamide added since the ED proposal has now been legally adopted
DBNPA added since the ED proposal has now been legally adopted
Asulam added since the ED proposal has now been legally adopted
Benthiavalicarb added since the ED proposal has now been legally adopted
Dimethomorph added since the ED proposal has now been legally adopted
Metiram added since the ED proposal has now been legally adopted
Mepanipyrim added since the ED proposal has now been legally adopted
Clofentezine added since the ED proposal has now been legally adopted
Triflusulfuron-methyl added since the ED proposal has now been legally adopted
List II
Propiconazole removed (added to list I)
Cyanamide removed (added to list I)
DBNPA removed (added to list I)
Asulam removed (added to list I)
Benthiavalicarb removed (added to list I)
Dimethomorph removed (added to list I)
Metiram removed (added to list I)
Mepanipyrim removed (added to list I)

Clofentezine removed (added to list I)
Triflusulfuron-methyl removed (added to list I)
Sodium Fluoride added: ED HH CLH intention submitted
3-aminopropyldiethylamine added: ED HH CLH intention submitted
Mono- and di-phthalate esters with linear and/or branched alkyl moieties with at least one longest continuous carbon chain counted from the ester function corresponding to C4-C6 and/or with C6 cyclic saturated carbon chains and/or with unsaturated hydrocarbyl moieties added: ED HH and ENV CLH intention submitted
Tris(4-nonylphenyl, branched) phosphite: SVHC ED ENV intention submitted. This intention addresses the group of substances "Tris(4-nonylphenyl, branched) phosphite".
1,1'-[ethane-1,2-diylbisoxy]bis[2,4,6-tribromobenzene] removed: SVHC ED intention no longer available
Thiophanate-methyl added: Concluded ED in EFSA opinion. Not yet legally adopted.
4,4'-isopropylidenedi-2,6-xylol added: Substance evaluation under REACH initiated (CoRAP)
4,4'-isopropylidenebis[2-allylphenol] added: Substance evaluation under REACH initiated (CoRAP)
2,4,6-tribromophenol added: Substance evaluation under REACH initiated (CoRAP)
2,2'-[(1-methylethylidene)bis(4,1-phenyleneoxy)]bisethyl diacetate added: Substance evaluation under REACH initiated (CoRAP)
(1-methylethylidene)bis(4,1-phenyleneoxy-3,1-propanediyl) bismethacrylate added: Substance evaluation under REACH initiated (CoRAP)
Tris[2-chloro-1-(chloromethyl)ethyl] phosphate removed: Withdrawn from CoRAP
4-tert-butylphenol removed: REACH substance evaluation concluded ED ENV (already on list I) + ED HH unresolved.
2-Ethylhexyl trans-4-methoxycinnamate removed: Substance evaluation concluded: ED inconclusive.
Benzophenone-4 removed: SCCS evaluation finalised.
Butylparaben removed: SCCS evaluation finalised: Still on list I
Benzyl salicylate removed: SCCS evaluation finalised
List III
Reaction products of phosphoryl trichloride and 2-methyloxirane (TCPP). Added by Denmark (evaluated as ED for HH)
https://edlists.org/about-this-site/list-updates

Endocrine disruptor assessment list,
ECHA (juin 2024),
Latest updates with Status Concluded in 2024
Diuron (ED Env, ED HH inconclusive) ; Sodium perfluoroheptanoate (inconclusive) ; Formic acid (not ED) ; Phenol, methylstyrenated (ED ENV) ; p-(1,1-dimethylpropyl)phenol (ED ENV, ED HH inconclusive) ; Diethylmethylbenzenediamine (inconclusive) ; Benzotriazole (ED ENV) ; 4-tert-butylphenol (ED ENV, ED HH inconclusive). https://echa.europa.eu

Essai n° 493 : Ligne directrice axée sur la performance pour les essais in vitro faisant appel au récepteur d'oestrogène recombinant humain (hrER) pour la détection des substances ayant une affinité de liaison avec les récepteurs des oestrogènes,
(25 juin 2024): 66 pages,
La présente Ligne directrice pour les essais axée sur la performance (LDAP) décrit la méthodologie des essais in vitro faisant appel au récepteur d'œstrogène recombinant humain pour la détection des substances ayant une affinité de liaison avec les récepteurs des œstrogènes (essais de liaison au hrER). Elle comprend deux méthodes d'essai structurellement et fonctionnellement similaires pour détecter les ligands des récepteurs des œstrogènes (ERα), et doit faciliter l'élaboration de nouvelles méthodes similaires ou modifiées. La base de la présente LDAP est constituée de deux méthodes d'essai de référence. Ces deux méthodes sont les suivantes: l'essai de Freyberger-Wilson (FW), essai in vitro de liaison aux ER à l'aide d'un ERα humain intégral et l'essai du Chemical Evaluation and Research Institute (CERI), essai in vitro de liaison aux ER à l'aide du domaine de liaison du ligand d'un ER recombinant humain. Cet essai consiste principalement à mesurer la capacité d'un ligand radiomarqué (le [3H]-17β-œstradiol) à se lier aux ER en présence de concentrations croissantes du produit chimique testé (appelé « compétiteur »). Les produits chimiques d'essai qui présentent une forte affinité de liaison avec les ER entrent en concurrence avec le ligand radiomarqué à une concentration plus faible que les composés ayant une affinité moindre vis-à -vis

du récepteur. L'essai comporte deux grands éléments : une expérience de liaison à saturation pour établir les paramètres de l'interaction récepteur-ligand et documenter la spécificité des liaisons aux ER, puis une expérience de liaison compétitive visant à déterminer dans quelle mesure un produit chimique testé fait concurrence à un ligand radiomarqué pour se fixer aux ER. Les présentes méthodes sont proposées à des fins de dépistage et de priorisation, mais elles peuvent aussi livrer des informations sur les mécanismes d'action pouvant être utilisées dans le cadre d'une approche fondée sur le poids de la preuve. https://www.oecd-ilibrary.org/fr/environment/essai-n-493-ligne-directrice-axee-sur-la-performance-pour-les-essais-in-vitro-faisant-appel-au-recepteur-d-oestrogene-recombinant-humain-hrer-pour-la-detection-des-substances-ayant-une-affinite-de-liaison-avec-les-recepteurs-des-oestrogenes_9789264242630-fr

Essai No. 252 : Essai rapide d'activité estrogen in vivo (REACTIV, Rapid Estrogen ACTivity In Vivo), *Ocde* (25 juin 2024): 52 pages,
La présente Ligne directrice relative à l'essai REACTIV (Rapid Estrogen ACTivity In Vivo) décrit un essai aquatique faisant appel à des éleuthéroembryons d'Oryzias latipes (médaka japonais) transgénique au jour zéro après éclosion, dans un format multipuits, afin d'identifier les produits chimiques agissant sur l'axe œstrogénique. La méthode REACTIV a été conçue comme un outil de dépistage assurant un débit moyen pour des essais à court terme visant à mesurer la réponse d'éleuthéroembryons à des produits chimiques potentiellement actifs sur l'axe œstrogénique. https://www.oecd-ilibrary.org/fr/environment/essai-no-252-essai-rapide-d-activite-estrogen-in-vivo-reactiv-rapid-estrogen-activity-in-vivo_903c3247-fr

Étude PEPS'PE : priorisation des effets sanitaires à surveiller dans le cadre du programme de surveillance en lien avec les perturbateurs endocriniens. Résultats,
SPF, *Santé Publique France* (octobre 2023),
L'objectif de l'étude PEPS'PE était de prioriser les effets sanitaires à surveiller dans le contexte d'une exposition aux PE grâce à la consultation d'experts et de parties prenantes du champ des PE, sur la base de critères scientifiques et sociétaux, afin de cadrer le programme de surveillance en lien avec les PE de Santé publique France. La méthodologie a fait l'objet d'un rapport déjà publié en 2021 et ce rapport présente les résultats de cette première étape de priorisation via la méthode de consensus Delphi. https://www.santepubliquefrance.fr/determinants-de-sante/exposition-a-des-substances-chimiques/perturbateurs-endocriniens/documents/enquetes-etudes/etude-peps-pe-priorisation-des-effets-sanitaires-a-surveiller-dans-le-cadre-du-programme-de-surveillance-en-lien-avec-les-perturbateurs-endocrini

Évaluation de la deuxième stratégie nationale sur les perturbateurs endocriniens - Pour une future stratégie « zéro exposition aux perturbateurs endocriniens » | IGEDD,
(2024-07-08 2024),
Adoptée en septembre 2019, la deuxième stratégie nationale sur les perturbateurs endocriniens (SNPE2) a pour ambition de réduire l'exposition de la population et de l'environnement aux PE. Son plan d'action s'articule autour de 3 volets : « Former et informer » (13 actions), « Protéger la population et l'environnement » (28 actions) et « Améliorer les connaissances » (9 actions).Les lacunes du dispositif de surveillance et le manque de suivi des indicateurs de la SNPE2 ne permettent pas d'apprécier l'atteinte – ou non – de son objectif premier : réduire l'exposition de la population et de l'environnement aux perturbateurs endocriniens. La mission considère néanmoins que cette stratégie est globalement pertinente, en adéquation avec les enjeux liés aux perturbateurs endocriniens, bien qu' insuffisamment tournée vers une réduction effective de l'exposition aux PE. Compte tenu des risques que les perturbateurs endocriniens font peser sur la

santé humaine et celle des écosystèmes, la mission recommande de poursuivre et d'amplifier la dynamique impulsée par les deux premières stratégies. Cette action gagnerait à s'inscrire dans une stratégie « Une seule santé » (ou une « Stratégie nationale santé environnement ») bénéficiant d'un pilotage interministériel au plus haut niveau. A défaut d'une telle stratégie globale, la mission recommande d'élaborer une 3ème version de la stratégie nationale sur les perturbateurs endocriniens (SNPE3) structurée autour de 3 grands objectifs : Produire des connaissances ; Former et informer ; Réduire les émissions. En matière de gouvernance, le succès de la SNPE3 nécessite un engagement de tous les ministères, y compris au niveau politique. Le plan d'action adossé à la SNPE3 doit être doté d'un budget pluriannuel, incluant des financements consacrés à la mise en œuvre d'actions nouvelles et spécifiques aux PE, en complément des moyens déjà prévus ou engagés. https://www.igedd.developpement-durable.gouv.fr/evaluation-de-la-deuxieme-strategie-nationale-sur-a4021.html

De nouveaux regards sur les perturbateurs endocriniens,
Anr (juin 2024),
Le 13 juin dernier, à la Maison de la RATP, à Paris, l'ANR et l'Anses organisaient une Journée d'échanges sur les dernières avancées de la recherche sur la problématique majeure des perturbateurs endocriniens. Cet article présente rapidement les sujets traités lors de cette journée et les projets en cours. Un dépliant a été réalisé également pour présenter les projets de l'ANR sur la période 2005-2023. https://anr.fr/fileadmin/documents/2024/ANR-brochure-perturbateurs-endocriniens-2024.pdf

Dossier : Perturbateurs endocriniens · Des risques potentiels ou avérés pour la santé humaine,
INSERM, *Inserm* (mai 2024 2024),
Les perturbateurs endocriniens regroupent une vaste famille de composés capables d'interagir avec le système hormonal. Les données scientifiques suggèrent qu'ils peuvent altérer de nombreuses fonctions de l'organisme (métabolisme, fonctions reproductrices, système nerveux…) mais leurs effets sur la santé humaine sont complexes à évaluer. L'étude des perturbateurs endocriniens représente aujourd'hui un enjeu majeur pour le corps médical et les pouvoirs publics, dans un souci de protection des populations vulnérables. https://www.inserm.fr/dossier/perturbateurs-endocriniens/

FREIA recommendations to protect women's health against endocrine disrupting chemicals,
Freia Project (juillet 2024),
Endocrine disrupting chemicals (EDCs) pose significant threats to women's reproductive health. Following five years of research, the FREIA project has published recommendations for health promotion strategies and EU-wide policy action to reduce exposure.
http://freiaproject.eu/wp/release/freia-recommendations-to-protect-womens-health-against-endocrine-disrupting-chemicals/

Glyphosate : la Commission européenne rejette la demande d'annulation de la réapprobation, des ONG s'adressent au tribunal européen - Générations Futures,
Générations Futures (2024-06-27 2024),
Le 26 juin 2024, la Commission européenne a rejeté la demande formelle de PAN Europe et de cinq de ses ONG membres (dont Générations Futures) de réexaminer la réapprobation de 10 ans du glyphosate. Les ONG prévoient de contester la décision devant les tribunaux et disposent de 2 mois pour introduire un recours en justice. https://www.generations-futures.fr/actualites/glyphosate-tribunal-ue/

HEEDS – Healthy Environment and Endocrine Disruptor Strategies (Plate-forme d'échange et d'information sur les PE à destination des scientifiques.
Une newsletter est également proposée : https://heeds.org/heeds-newsletter/ https://heeds.org/

Les perturbateurs endocriniens, un défi scientifique,
Anses (2024-06-12 2024),
Les perturbateurs endocriniens sont des substances capables d'interférer avec notre système hormonal, provoquant des effets délétères pour notre santé. Face aux multiples sources d'exposition, l'enjeu est de pouvoir comprendre le rôle joué par ces substances dans le développement de certaines pathologies. https://www.anses.fr/fr/content/les-perturbateurs-endocriniens-un-defi-scientifique

Les travaux de l'Anses pour mieux connaitre les perturbateurs endocriniens,
Anses (2024-06-12 2024),
De nombreuses substances sont suspectées de perturber le système endocrinien, telles que les bisphénols, les phtalates, les parabènes, les composés bromés et perfluorés ou encore les alkylphénols. Depuis de nombreuses années, l'Anses mène un important travail pour évaluer les substances chimiques ayant des propriétés potentielles de perturbation endocrinienne. Elle finance également des recherches pour mieux connaître les effets et les mécanismes d'action de ces substances et évalue l'exposition de la population. https://www.anses.fr/fr/content/travaux-anses-sur-perturbateurs-endocriniens

MERLON (Merging scientific evidence with regulatory practices and leveraging identification of endocrine disruptors using new approach methodologies),
(2024),
MERLON is a five-year project that explores how endocrine disrupting chemicals (EDCs) impact health. The project will also develop tools for chemical risk assessors and policymakers to better identify and ultimately regulate EDCs. The MERLON project brings together world-leading experts from 11 partner institutions across Europe. https://merlon.dtu.dk/

New substance evaluation conclusion published for CoRAP substance : Diuron,
ECHA (juin 2024),
Diuron (EC 206-354-4, CAS 330-54-1), was added to the Community rolling action plan (CoRAP) list in 2014 and evaluated by Finland. Initial grounds for concern : Potential endocrine disruptor ; Other exposure/risk based concern ; Wide dispersive use. Conclusion Document (juin 2024) : Based on the available information, the evaluating MSCA considers that Diuron can be classified as endocrine disruptor for the environment in Category 1. The concern for endocrine disruption (human health) can be considered inconclusive as the information available is neither sufficient for identifying the Substance as an endocrine disruptor for human health nor for excluding the concern. However, the evaluating MSCA considers that due to the ongoing ED assessment under Biocidal Products Regulation and the fact that the ED concern is confirmed for the environment, it is currently not justified to request further information under REACH Regulation. The evaluating MSCA considers that a classification of the Substance as an ED for human health would be unlikely to result in further risk management measures compared to the obligations coming from the classification as Carc. 1B in Commission Delegated Regulation (EU) 2024/197. https://echa.europa.eu/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table/-/dislist/details/0b0236e180697276#msdynttrid=0YbKgAl9rHbIx4FdaQOpFHZ3EzWxjx7-x70dHobdwPE

Podcast - Les Pfas, c'est quoi ? Comprendre les polluants éternels, leur impact sur la santé et comment s'en protéger - Vidéo - INRS,
Inrs (2024),
Les Pfas sont des substances chimiques qui ont pour particularité de se dégrader très peu, c'est pourquoi elles sont désignées également sous le terme de "polluants éternels" ou encore "produits chimiques éternels". Mais quels risques sont encourus lors de la production ou de l'utilisation de ses Pfas ? Quels sont les moyens de protection à mettre en oeuvre pour se protéger de ces polluants éternels ? Les explications de Myriam Ricaud, experte d'assistance-conseil à l'INRS.
https://www.inrs.fr/media.html?refINRS=Anim-408

Présentations du la conference 2024 EURION (du 14 juin 24 à Bruxelles),
(2024),
Résumé : https://ergo-project.eu/ergo-at-the-eurion-final-conference-2024/
Présentations : https://ergo-project.eu/results/presentations/

Press release announcing the start of the ENDOMIX project,
ENDOMIX (janvier 2024),
New EU project sheds light on the interplay between endocrine disrupting chemicals and human health. The EU-funded research project ENDOMIX started January 1st and aims to comprehensively unravel how exposure to everyday chemicals with endocrine disrupting properties affect human health. The researchers will also elaborate recommendations to reduce exposure to these chemicals and minimize thereby health risks. ENDOMIX runs until the end of 2027 and is funded by the European Union's Horizon Europe research and innovation programme.
https://endomix.eu/wp-content/uploads/2024/03/240115_press-release_ENDOMIX_EN.pdf

Project information. Network for Cross-disciplinary assessment of Endocrine Disrupting compounds: training the next generation of toxicologists (NeXED),
(Project Period : 1/2025 - 12/2028. Investor / Pogramme / Project type : European Union.
The EU has flagged endocrine disrupting chemicals (EDCs), which interfere with normal hormonal function leading to adverse health effects, of particular concern. Within different EU regulatory programmes the assessment of EDCs has recently changed significantly and continues to evolve rapidly. Advances in test methods for assessment of EDCs are needed to meet these changing regulatory requirements, and a new generation of toxicologists must be trained to support the implementation of the most advanced approaches. NeXED will address three critical challenges in this area. First, human and environmental EDC assessment have historically been separate disciplines while there is an increasing need to use data across species in a One Health approach. Second, EDC assessment currently addresses single compounds while in an environmentally realistic scenario organisms are faced with complex mixtures of EDCs. Third, new test methods for EDC assessment are needed, covering less well-characterised mechanisms and effects. NeXED aims to facilitate a paradigm shift in EDC assessment by training a new generation of cross-disciplinary toxicologists specialised in using harmonised approaches in a One Health framework. NeXED will train its 14 doctoral candidates through research, secondments and training events using an interdisciplinary and intersectoral training programme. NeXED brings together 10 Beneficiaries and 10 Associated Partners from 10 countries, building upon long-standing collaborations through existing projects including the Horizon 2020 EURION projects and the Horizon Europe Partnership on the Assessment of Risk from Chemicals (PARC). The consortium includes leading researchers from institutions with excellent doctoral training programmes who are all experts in ED assessment,

as well as industry partners, regulatory agencies, SMEs and consultancy firms. With its complementary expertise the consortium is ideally placed to train the NeXED generation of toxicologists. https://www.labifel.sci.muni.cz/en/research/current-projects/72266

Rapport "Prioritisation of Endocrine Disruptors for Regulation" *CeHoS - Center for Hormonforstyrrende Stoffer (Danemark)* (2024),
Dans le cadre d'un projet CeHoS, des chercheurs du DTU Food Institute et de l'Université du Danemark du Sud ont examiné la littérature pour trouver des substances présentant des signes de propriétés perturbatrices des hormones. Dans l'étude, les chercheurs ont constaté un manque généralisé de données, notamment en ce qui concerne les effets sur l'environnement. Les chercheurs soulignent que ce manque de données est profondément problématique et qu'il est absolument nécessaire de mettre à jour les exigences en matière d'information dans la législation européenne REACH afin qu'elles incluent des informations sur les propriétés perturbateurs endocriniens. Dans l'UE, la réduction de l'exposition des personnes et de l'environnement aux substances perturbant le système hormonal constitue une priorité absolue. Cependant, les données communiquées par les entreprises dans le cadre de la législation européenne sur les produits chimiques industriels, REACH, contiennent rarement des informations pouvant être utilisées pour évaluer si les substances sont des perturbateurs endocriniens dans l'environnement. Pour 70 % des plus de 26 000 produits chimiques industriels utilisés dans toutes sortes de produits différents, il n'existe également aucune information permettant d'évaluer si ces substances sont des perturbateurs endocriniens pour l'homme.
Les chercheurs recommandent donc que toutes les informations disponibles soient utilisées au mieux selon deux approches :
1. En évaluant des substances similaires les unes aux autres en tant que groupe unifié
2. En appliquant les connaissances sur les effets nocifs à toutes les espèces
La nouvelle étude s'appuie sur un rapport du CeHoS de 2018 , qui désignait une liste de base de 171 substances. Dans la nouvelle étude, la liste de base a été étendue à 192 substances. À l'aide d'une série de critères d'exclusion, les 192 substances ont été filtrées en 97 substances ciblées, dont 10 ont été sélectionnées pour une analyse documentaire. Lors de l'examen de la littérature, les chercheurs ont découvert des propriétés perturbatrices endocriniennes pour 9 substances sur 10 qui, entre autres, utilisé dans les cosmétiques et les produits de consommation. Les chercheurs à l'origine de l'étude soulignent qu'il ne s'agit que d'un premier examen de la littérature et qu'une évaluation plus approfondie des données disponibles est nécessaire avant de pouvoir tirer des conclusions définitives sur les substances étudiées.
L'Agence danoise de protection de l'environnement a soutenu le projet car la documentation scientifique peut être utilisée pour influencer la réglementation européenne afin qu'elle protège mieux les consommateurs et l'environnement qu'auparavant. https://www.cend.dk/files/ED-list_II_2024.pdf

Actualité : Société

Occitanie : lancement d'une étude sur la présence des perturbateurs endocriniens dans l'air, INDÉPENDANTE L. O., *L'Opinion Indépendante* (05 juin 2024),
Atmo Occitanie a annoncé le lancement d'une étude exploratoire de trois ans sur la présence de perturbateurs endocriniens dans l'air. Depuis le mois de mars 2024 et pour les prochaines années, l'organisme de surveillance de la qualité de l'air va donc se pencher sur le sujet. "Cette étude d'envergure est une première en France. Pour la première fois, sera évaluée à l'échelle régionale, l'évolution de la présence de molécules à caractère perturbateur endocrinien sur une longue période, dans différents environnements".

https://lopinion.com/articles/actualite/23560_occitanie-lancement-etude-presence-perturbateurs-endocriniens-air

Perturbateurs endocriniens : la Ville de Besançon lance un guide pratique,
MACOMMUNE, (2024),
Dans un communiqué du 15 avril 2024, la Ville de Besançon annonce la disponibilité d'un guide pratique afin de sensibiliser, d'informer la population à l'exposition aux perturbateurs endocriniens et adopter les bons gestes. https://www.macommune.info/perturbateurs-endocriniens-la-ville-de-besancon-lance-un-guide-pratique/

Généralités et stratégies de prévention

Assessing preconception exposure to environmental chemicals and fecundity: Strategies, challenges, and research priorities,
ASHLEY-MARTIN J., J. HAMMOND and M. P. VELEZ, *Reproductive Toxicology* 125 (Apr 2024),
In 2022, approximately one out of six people globally experienced infertility at some point in their life. Environmental chemicals, particularly those with endocrine disrupting activity, may contribute to impaired fecundity and infertility. We review existing prospective cohort studies of environmental chemicals and fecundity, identify methodological challenges and biases, and outline future research priorities. Studies of preconception environmental chemical exposures and fecundity have occurred in US, Singapore, China and Denmark with recruitment as early as 1982 - 1986, as recent as 2015 -2017 and sample sizes ranging from 99 to 936. Higher exposure to certain chemicals (e.g. heavy metals, perfluoroalkyl substances) was associated with longer time to pregnancy; yet the literature is scarce or nonexistent for many chemicals. Furthermore, prospective studies face challenges and potential biases related to recruiting participants prior to conception, measuring environmental chemicals during critical windows of exposure, and ascertaining when pregnancy occurred. Research priorities include expanding the scope of biomonitoring data collected during the preconception period, continuing to develop and validate analytic methods for self -sampled biospecimens in traditional and novel matrices, collecting data in male partners and investigating etiologic associations according to indicators of marginalization.
https://doi.org/10.1016/j.reprotox.2024.108578

The Conflict between Regulatory Agencies over the 20,000-Fold Lowering of the Tolerable Daily Intake (TDI) for Bisphenol A (BPA) by the European Food Safety Authority (EFSA),
VOM SAAL F. S., M. ANTONIOU, S. M. BELCHER et COLL, *Environmental Health Perspectives* 132, no. 4 (Apr 2024),
BACKGROUND: The European Food Safety Authority (EFSA) recommended lowering their estimated tolerable daily intake (TDI) for bisphenol A (BPA) 20,000-fold to 0:2 ng/kg body weight & eth;BW & THORN;/day. BPA is an extensively studied high production volume endocrine disrupting chemical (EDC) associated with a vast array of diseases. Prior risk assessments of BPA by EFSA as well as the US Food and Drug Administration (FDA) have relied on industry-funded studies conducted under good laboratory practice protocols (GLP) requiring guideline end points and detailed record keeping, while also claiming to examine (but rejecting) thousands of published findings by academic scientists. Guideline protocols initially formalized in the mid -twentieth century are still used by many regulatory agencies. EFSA used a 21st century approach in its reassessment of BPA and conducted a transparent, but time -limited, systematic review that included both guideline and academic research. The German Federal Institute for Risk Assessment (BfR) opposed EFSA's revision of the TDI for BPA. OBJECTIVES : We identify the flaws in the assumptions that the German BfR, as

well as the FDA, have used to justify maintaining the TDI for BPA at levels above what a vast amount of academic research shows to cause harm. We argue that regulatory agencies need to incorporate 21st century science into chemical hazard identifications using the CLARITY-BPA (Consortium Linking Academic and Regulatory Insights on BPA Toxicity) nonguideline academic studies in a collaborative government-academic program model. DISCUSSION : We strongly endorse EFSA's revised TDI for BPA and support the European Commission's (EC) apparent acceptance of this updated BPA risk assessment. We discuss challenges to current chemical risk assessment assumptions about EDCs that need to be addressed by regulatory agencies to, in our opinion, become truly protective of public health. Addressing these challenges will hopefully result in BPA, and eventually other structurally similar bisphenols (called regrettable substitutions) for which there are known adverse effects, being eliminated from all food -related and many other uses in the EU and elsewhere. https://doi.org/10.1289/EHP13812 https://doi.org/10.1289/ehp13812

Effects of Behavioral, Clinical, and Policy Interventions in Reducing Human Exposure to Bisphenols and Phthalates: A Scoping Review,
SIECK N. E., M. BRUENING, I. VAN WOERDEN, C. WHISNER and D. C. PAYNE-STURGES, *Environmental Health Perspectives* 132, no. 3 (Mar 2024),
B ACKGROUND : There is growing interest in evidence -based interventions, programs, and policies to mitigate exposures to bisphenols and phthalates and in using implementation science frameworks to evaluate hypotheses regarding the importance of specific approaches to individual or household behavior change or institutions adopting interventions. O BJECTIVES : This scoping review aimed to identify, categorize, and summarize the effects of behavioral, clinical, and policy interventions focused on exposure to the most widely used and studied bisphenols [bisphenol A (BPA), bisphenol S (BPS), and bisphenol F (BPF)] and phthalates with an implementation science lens. M ETHODS : A comprehensive search of all individual behavior, clinical, and policy interventions to reduce exposure to bisphenols and phthalates was conducted using PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and Google Scholar. We included studies published between January 2000 and November 2022. Two reviewers screened references in CADIMA, then extracted data (population characteristics, intervention design, chemicals assessed, and outcomes) for studies meeting inclusion criteria for the present review. R ESULTS : A total of 58 interventions met the inclusion criteria. We classified interventions as dietary (n = 27), clinical (n = 13), policy (n = 14), and those falling outside of these three categories as "other" (n = 4). Most interventions (81%, 47/58) demonstrated a decrease in exposure to bisphenols and/or phthalates, with policy level interventions having the largest magnitude of effect. D ISCUSSION : Studies evaluating policy interventions that targeted the reduction of phthalates and BPA in goods and packaging showed widespread, longterm impact on decreasing exposure to bisphenols and phthalates. Clinical interventions removing bisphenol and phthalate materials from medical devices and equipment showed overall reductions in exposure biomarkers. Dietary interventions tended to lower exposure with the greatest magnitude of effect in trials where fresh foods were provided to participants. The lower exposure reductions observed in pragmatic nutrition education trials and the lack of diversity (sociodemographic backgrounds) present limitations for generalizability to all populations. https://doi.org/10.1289/EHP11760 https://doi.org/10.1289/ehp11760

Empowering Student Pharmacists to Counsel Patients on Endocrine Disrupting Chemicals through Interactive Role-Play,
CERNASEV A., A. HALL, S. THOMAS-GOOCH and D. SCOTT, *Pharmacy* 12, no. 2 (Apr 2024),
Preparing the next generation of pharmacists to succeed in practice and provide premier care starts with ensuring pharmacy education standards are met and align with innovative practices and that

education incorporates topics that are important to promoting health. For example, recent reports link endocrine disrupting chemicals (EDCs) to numerous diseases such as reproductive disorders, metabolic diseases, and developmental abnormalities. Considering the suboptimal awareness and knowledge about EDCs, it is imperative to provide public health education through a pharmacy curriculum. The objective of this study was to evaluate student pharmacists' perceptions of the impact of a role play activity on their knowledge of EDCs and counseling skills. A secondary objective was to explore student pharmacists' perceptions of how role play might impact their future career as a pharmacist. A retrospective qualitative study consisting of a lecture, a pre-brief, a low-fidelity simulation centered on role-play, and debrief to develop knowledge of EDCs to practice counseling skills, and a post reflection was implemented to explore this aim. Third year student pharmacists who were enrolled on the public health elective course were eligible to participate in the study. All reflections were de-identified, imported into a qualitative software, Dedoose (R), Version 9.2.6 and thematically analyzed using an inductive approach. Thematic analysis revealed three master themes, which tell the story of an initial lack of familiarity with EDCs that was rectified by the lecture and low-fidelity simulation. In the first theme, we can see that all of the participants noted their positive perceptions of the low-fidelity simulation, especially the role playing on a topic they lacked familiarity with. In the second theme, participants revealed the activity's impact on their performance or behaviors. Finally, the third theme explores the future implications of a pharmacist's impact on public health. This novel study contributes to a growing body of literature on the impact of pharmacy education practices and instruction on public health. The findings suggest that pharmacy educators might consider incorporating role playing instruction for public health topics, EDCs, or topics not traditionally taught in the pharmacy curriculum.
https://doi.org/10.3390/pharmacy12020055

Endocrine disruption and male reproductive disorders: unanswered questions,
SHARPE R. M., *Human Reproduction* (2024 Jun 2024),
Maternal exposure to endocrine-disrupting chemicals (EDCs) in human pregnancy is widely considered as an important cause of adverse changes in male reproductive health due to impaired foetal androgen production/action. However, the epidemiological evidence supporting this view is equivocal, except for certain phthalates, notably diethyl hexyl phthalate (DEHP). Maternal phthalate exposure levels associated with adverse reproductive changes in epidemiological studies are several thousand-fold lower than those needed to suppress foetal androgen production in rats, and direct studies using human foetal testis tissue show no effect of high phthalate exposure on androgen production. This conundrum is unexplained and raises fundamental questions. Human DEHP exposure is predominantly via food with highest exposure associated with consumption of a Western style (unhealthy) diet. This diet is also associated with increased exposure to the most common EDCs, whether persistent (chlorinated or fluorinated chemicals) or non-persistent (phthalates, bisphenols) compounds, which are found at highest levels in fatty and processed foods. Consequently, epidemiological studies associating EDC exposure and male reproductive health disorders are confounded by potential dietary effects, and vice versa. A Western diet/lifestyle in young adulthood is also associated with low sperm counts. Disentangling EDC and dietary effects in epidemiological studies is challenging. In pregnancy, a Western diet, EDC exposure, and maternal living in proximity to industrial sites are all associated with impaired foetal growth/development due to placental dysfunction, which predisposes to congenital male reproductive disorders (cryptorchidism, hypospadias). While the latter are considered to reflect impaired foetal androgen production, effects resulting from foetal growth impairment (FGI) are likely indirect. As FGI has numerous life-long health consequences, and is affected by maternal lifestyle, research into the origins of male reproductive disorders should take more account of this. Additionally, potential effects on foetal growth/foetal testis from the increasing use of medications in pregnancy deserves more research attention. Graphical Abstract Pathways via which diet and exposure to endocrine-

disrupting chemicals, medicines, and industrial pollution can inter-connect to affect reproductive development/health of men. EDCs, endocrine-disrupting chemicals.
https://doi.org/10.1093/humrep/deae143

Exploring BPA alternatives - Environmental levels and toxicity review,
ADAMOVSKY O., K. J. GROH, A. BIALK-BIELINSKA, B. I. ESCHER, R. BEAUDOUIN, L. M. LAGARES, K. E. TOLLEFSEN, M. FENSKE, E. MULKIEWICZ, N. CREUSOT, A. SOSNOWSKA, S. LOUREIRO, J. BEYER, G. REPETTO, A. STERN, I. LOPES, M. MONTEIRO, A. ZIKOVA-KLOAS, T. ELERSEK, M. VRACKO, S. ZDYBEL, T. PUZYN, W. KOCZUR, J. E. MORTHORST, H. HOLBECH, G. CARLSSON, S. ORN, O. HERRERO, A. SIDDIQUE, M. LIESS, G. BRAUN, V. SREBNY, B. ZEGURA, N. HINFRAY, F. BRION, D. KNAPEN, E. VANDEPUTTE, E. STINCKENS, L. VERGAUWEN, L. BEHRENDT, M. J. SILVA, L. BLAHA and K. KYRIAKOPOULOU, *Environment International* 189 (Jul 2024),
Bisphenol A alternatives are manufactured as potentially less harmful substitutes of bisphenol A (BPA) that offer similar functionality. These alternatives are already in the market, entering the environment and thus raising ecological concerns. However, it can be expected that levels of BPA alternatives will dominate in the future, they are limited information on their environmental safety. The EU PARC project highlights BPA alternatives as priority chemicals and consolidates information on BPA alternatives, with a focus on environmental relevance and on the identification of the research gaps. The review highlighted aspects and future perspectives. In brief, an extension of environmental monitoring is crucial, extending it to cover BPA alternatives to track their levels and facilitate the timely implementation of mitigation measures. The biological activity has been studied for BPA alternatives, but in a non-systematic way and prioritized a limited number of chemicals. For several BPA alternatives, the data has already provided substantial evidence regarding their potential harm to the environment. We stress the importance of conducting more comprehensive assessments that go beyond the traditional reproductive studies and focus on overlooked relevant endpoints. Future research should also consider mixture effects, realistic environmental concentrations, and the long-term consequences on biota and ecosystems.
https://doi.org/10.1016/j.envint.2024.108728

Impacts de la crise environnementale et climatique sur la santé de la femme : quelles spécificités ? Que peut-on faire ?,
AZOULAY C., *Gynécologie Obstétrique Fertilité & Sénologie* (2024/03/15/ 2024),
Résumé Objectif La pollution représente l'un des principaux facteurs de risque de maladie et de décès prématuré à l'échelle planétaire. En Europe, on lui attribue près de 20 % de la mortalité. La pollution chimique se fait par la respiration, l'ingestion ou contact cutané et elle commence in utero. Les polluants se répartissent en 3 catégories : les perturbateurs endocriniens (pesticides, PFAS, plastiques, dioxines…), les métaux lourds (cadmium, mercure et plomb…) et les nanomatériaux. Le dérèglement climatique et la pollution de l'air sont la deuxième principale menace sanitaire. Méthodes Revue de la littérature par interrogation des bases PubMed, ResearchGate et des sites institutionnels. Résultats Les principaux risques des perturbateurs endocriniens concernent la santé reproductive et l'impact d'une exposition pré-conceptionnelle, périnatale ou à l'âge adulte est documenté dans la littérature. Le dérèglement climatique et la pollution de l'air provoquent des pathologies genrées et non genrées. De plus en plus d'arguments scientifiques convergent aujourd'hui sur le fait que la pollution chimique et le dérèglement climatique impactent beaucoup plus les femmes que les hommes, aussi bien sur un plan social que biologique. Les populations en situation de précarité, parmi lesquelles les femmes sont surreprésentées, y compris en France, sont celles qui subissent les conséquences sociales les plus sévères. Les expositions sexo-spécifiques domestiques ou professionnelles aux polluants sont nombreuses, le plus souvent en défaveur des femmes par rapport aux hommes. Enfin, bien que l'on dispose de peu de données genrées en santé environnementale, il existe des vulnérabilités

physiologiques vis-à-vis du métabolisme des polluants et de la capacité d'adaptation à la chaleur. Conclusion Devant cette menace d'augmentation des inégalités de genre en matière de santé et de droits sexuels et reproductifs, les professionnels de la santé féminine ont un rôle majeur à jouer pour initier des stratégies d'évaluation et de réduction du fardeau sanitaire environnemental chez les femmes. Objective Pollution is one of the world's largest risk factors for disease and premature death. In Europe, it is responsible for approximately 20% of mortality. Chemicals exposure can occur by inhalation, ingestion or skin contact and begins in utero. Pollutants can be divided into three categories: endocrine disruptors (pesticides, PFAS, plastics, dioxins, etc.), heavy metals (cadmium, mercury and lead…) and nanomaterials. Climate change and air pollution are other main health threats. Methods Literature review using PubMed and ResearchGate databases and institutional websites. Results Endocrine disruptors are identified as significant risk factors for the reproductive health with negative documented impacts following prenatal or adult exposure. Climate change and air pollution can cause gender-based health disparities. Numerous scientific arguments show that chemical pollution and climate change disproportionately impact women, both on a social and biological level. Populations in precarious situations among which women are over-represented suffer the most severe social consequences including in France. There are several gender-specific domestic or occupational exposures to pollutants, most often to the disadvantage of women compared to men. Finally, although very few gendered data exist in environmental health, there are sexual-based physiological vulnerabilities concerning the metabolism of pollutants and the capacity to adapt to heat. Conclusion Facing this threat of gender inequity in sexual and reproductive health and rights' width, women's health professionals have a major role to play in initiating new ways to assess and reduce the environmental health burden in women. https://doi.org/https://doi.org/10.1016/j.gofs.2024.03.004

Obesogens in Adolescence: Challenging Aspects and Prevention Strategies,
NICOLAOU M., M. TOUMBA, A. KYTHREOTIS, H. DAHER and N. SKORDIS, *Children-Basel* 11, no. 5 (May 2024),
Childhood obesity has become a global epidemic, with significant increases in prevalence over recent decades. While excessive calorie consumption and physical inactivity are known factors, emerging research highlights the role of endocrine-disrupting chemicals (EDCs), particularly obesogens, in obesity's pathogenesis. This review explores the historical context of the environmental obesogens hypothesis, their sources, mechanism of action, impact on prenatal and postnatal development, and epigenetics. Additionally, it discusses the long-term consequences of childhood obesity and proposes prevention strategies that will mitigate negative health effects. Obesogens were found to disrupt hormonal balance and metabolic processes through various mechanisms such as altering gene expression, hormonal interference, and inflammation. Especially significant was exposure during critical windows of development, which correlates with an increased risk of obesity in childhood or adolescence. Long-term effects of childhood obesity include chronic health conditions and psychosocial issues. A comprehensive approach is necessary to address childhood obesity encompassing genetic, environmental, and lifestyle factors. Prevention strategies should focus on reducing obesogen exposure, promoting healthy lifestyles, and implementing regulatory policies. Future research should investigate obesogens-diet interactions, microbiome impacts, and combined obesogens effects. Long-term human studies are also crucial for validating findings from animal models and allowing for informed decision-making to combat the obesity pandemic. https://doi.org/10.3390/children11050602

Perturbateurs endocriniens et environnement : quelles données utiliser ?,
CHAMOT S., L. LEROY, G. MARHIC, A. AL-SALAMEH, R. PONS, V. BONNETERRE, C. CANCÉ, M. RAMON-DARE, P. GRIGON, R. DESAILLOUD and P. PETIT, *Archives des Maladies Professionnelles et de l'Environnement* 85, no. 2 (2024/05/01/ 2024): 101943,

Résumé L'évaluation de l'impact sanitaire de l'exposition aux perturbateurs endocriniens, notamment environnementale, est une question majeure qui s'impose en matière de recherche clinique en santé publique. Pourtant, les difficultés sont nombreuses, tant pour identifier les substances à caractère perturbateur endocrinien que pour estimer les expositions qui y sont rattachées. C'est à ces deux problématiques que nous tenterons d'apporter un éclairage en présentant les différentes bases de données et les outils pertinents existants. Summary The health impact of exposure to endocrine disruptors is a major issue in public health research, particularly with regard to environmental exposure. However, there are many challenges, both in identifying endocrine disrupting substances and in estimating the exposures associated with these substances. We will attempt to address these two topics by presenting the available databases and tools that are relevant to tackle these issues. https://doi.org/https://doi.org/10.1016/j.admp.2023.101943

Pesticides impacts on human health and the environment with their mechanisms of action and possible countermeasures,
AHMAD M. F., F. A. AHMAD, A. A. ALSAYEGH, M. ZEYAULLAH, A. M. ALSHAHRANI, K. MUZAMMIL, A. A. SAATI, S. WAHAB, E. Y. ELBENDARY, N. KAMBAL, M. H. ABDELRAHMAN and S. HUSSAIN, *Heliyon* 10, no. 7 (Apr 2024),
Pesticides are chemical constituents used to prevent or control pests, including insects, rodents, fungi, weeds, and other unwanted organisms. Despite their advantages in crop production and disease management, the use of pesticides poses significant hazards to the environment and public health. Pesticide elements have now perpetually entered our atmosphere and subsequently contaminated water, food, and soil, leading to health threats ranging from acute to chronic toxicities. Pesticides can cause acute toxicity if a high dose is inhaled, ingested, or comes into contact with the skin or eyes, while prolonged or recurrent exposure to pesticides leads to chronic toxicity. Pesticides produce different types of toxicity, for instance, neurotoxicity, mutagenicity, carcinogenicity, teratogenicity, and endocrine disruption. The toxicity of a pesticide formulation may depend on the specific active ingredient and the presence of synergistic or inert compounds that can enhance or modify its toxicity. Safety concerns are the need of the hour to control contemporary pesticide-induced health hazards. The effectiveness and implementation of the current legislature in providing ample protection for human health and the environment are key concerns. This review explored a comprehensive summary of pesticides regarding their updated impacts on human health and advanced safety concerns with legislation. Implementing regulations, proper training, and education can help mitigate the negative impacts of pesticide use and promote safer and more sustainable agricultural practices. https://doi.org/10.1016/j.heliyon.2024.e29128

Pour une approche intégrée de la santé cérébrale,
Revue Médicale de Liège 76, no. 5-6 (2024): 311-318,
Le cerveau est un organe vital qui règle en partie notre homéostasie et régit nos interactions avec le monde (c'est-à-dire les environnements physiques, biologiques et sociaux). Un environnement sain et une société paisible et équitable assurent son développement normal et œuvrent au bien-être individuel (physique, mental, social et spirituel). Mais la santé cérébrale n'est jamais acquise et peut être détériorée, dès la conception et jusqu'au décès, par l'exposition à de multiples agents physiques, chimiques, biologiques, psychologiques et sociaux - l'exposome. Dans une perspective intégrée, cet article souligne la nécessité fondamentale de valoriser, promouvoir et protéger la santé du cerveau. Le défi actuel est de renforcer la sensibilisation, l'éducation et la recherche sur la santé cérébrale et prévenir les maladies neurologiques et psychiatriques.
https://rmlg.uliege.be/article/3920

Thresholds of adversity for endocrine disrupting substances: a conceptual case study,
CHOI J., S. ROTTER, V. RITZ, C. KNEUER, P. MARX-STOELTING, M. D. M. SOLANO, A. OERTEL, S. RUDZOK, A. ZIKOVÁ-KLOAS, T. TRALAU and A. HENSEL, *Archives of Toxicology* (2024 May 2024),
For endocrine disrupting chemicals (EDC) the existence of "safe exposure levels", that is exposure levels that do not present an appreciable risk to human health is most controversially discussed, as is the existence of health-based reference values. Concerns have been especially raised that EDCs might not possess a threshold level such that no exposure level to EDCs can be considered safe. To explore whether or not threshold levels can be identified, we performed a screening exercise on 14 pesticidal and biocidal active substances previously identified as EDCs in the European Union. The respective substances are ideal subjects for case studies to review for endocrine activity and disruptive potential following well-defined regulatory assessment based on solid data to effectually establish adversity as consequence of endocrine disruption. Dimethomorph, metiram and propiconazole for which the weight of evidence demonstrating endocrine disruption was the strongest were used as subjects for further study. Epoxiconazole was additionally selected as its effects on the endocrine system are extensive. For all four substances, analysis of the toxicological data clearly indicated thresholds of adversity below which no adverse effects mediated through an endocrine mechanism were observed. Particular emphasis was placed on mechanistic considerations including homeostasis and the concept of adversity. As a proof of concept this study provides evidence that like other substances of toxicological concern EDCs have threshold levels for adversity. While for some EDCs the respective thresholds might indeed be very low this shows that, data allowing, for other EDCs sufficiently protective reference values can be derived.
https://doi.org/10.1007/s00204-024-03748-9

Toxicité sur les animaux

Obesity aggravates neuroinflammatory and neurodegenerative effects of bisphenol A in female rats,
MANGLA A., P. GOSWAMI, B. SHARMA, S. SURAMYA, G. JINDAL, M. JAVED, M. A. SAIFI, S. PARVEZ, T. C. NAG and S. RAISUDDIN, *Toxicology Mechanisms and Methods* (2024 May 2024),
Bisphenol A (BPA), a common plasticizer, is categorized as a neurotoxic compound. Its impact on individuals exhibits sex-linked variations. Several biological and environmental factors impact the degree of toxicity. Moreover, nutritional factors have profound influence on toxicity outcome. BPA has been demonstrated to be an obesogen. However, research on the potential role of obesity as a confounding factor in BPA toxicity is lacking. We studied the neurodegenerative effects in high-fat diet (HFD)-induced obese female rats after exposure to BPA (10 mg/L via drinking water for 90 days). Four groups were taken in this study - Control, HFD, HFD + BPA and BPA. Cognitive function was evaluated through novel object recognition (NOR) test. Inflammatory changes in brain, and changes in hormonal level, lipid profile, glucose tolerance, oxidative stress, and antioxidants were also determined. HFD + BPA group rats showed a significant decline in memory function in NOR test. The cerebral cortex (CC) of the brain showed increased neurodegenerative changes as measured by microtubule-associated protein-2 (MAP-2) accompanied by histopathological confirmation. The increased level of neuroinflammation was demonstrated by microglial activation (Iba-1) and protein expression of nuclear factor- kappa B (NF-& Kcy;B) in the brain. Obesity also caused significant ($p < 0.05$) increase in lipid peroxidation accompanied by reduced activities of antioxidant enzymes (glutathione S-transferase, catalase and glutathione peroxidase) and decrease in reduced-glutathione ($p < 0.05$) when compared to non-obese rats with BPA treatment. Overall,

study revealed that obesity serves as a risk factor in the toxicity of BPA which may exacerbate the progression of neurological diseases. https://doi.org/10.1080/15376516.2024.2349538

Repeated-dose toxicity and toxicokinetic study of isobutylparaben in rats subcutaneously treated for 13 weeks,
LEE J. D., J. S. BAE, H. Y. KIM, S. W. SONG, J. C. KIM, B. M. LEE and K. B. KIM, *Archives of Toxicology* (2024 Apr 2024),
Parabens have historically served as antimicrobial preservatives in a range of consumables such as food, beverages, medications, and personal care products due to their broad-spectrum antibacterial and antifungal properties. Traditionally, these compounds were believed to exhibit low toxicity, causing minimal irritation, and possessing limited sensitization potential. However, recent evidence suggests that parabens might function as endocrine-disrupting chemicals (EDCs). Consequently, extensive research is underway to elucidate potential human health implications arising from exposure to these substances. Among these parabens, particular concerns have been raised regarding the potential adverse effects of iso-butylparaben (IBP). Studies have specifically highlighted its potential for inducing hormonal disruption, significant ocular damage, and allergic skin reactions. This study aimed to evaluate the prolonged systemic toxicity, semen quality, and estrus cycle in relation to endocrine disruption endpoints, alongside assessing the toxicokinetic behavior of IBP in Sprague-Dawley rats following a 13-week repeated subcutaneous administration. The rats were administered either the vehicle (4% Tween 80) or IBP at dosage levels of 2, 10, and 50 mg/kg/day for 13 weeks. Blood collection for toxicokinetic study was conducted on three specified days: day 1 (1st), day 30 (2nd), and day 91 (3rd). Systemic toxicity assessment and potential endocrine effects were based on various parameters including mortality rates, clinical signs, body weights, food and water consumption, ophthalmological findings, urinalysis, hematological and clinical biochemistry tests, organ weights, necropsy and histopathological findings, estrus cycle regularity, semen quality, and toxicokinetic behavior. The findings revealed that IBP induced local irritation at the injection site in males at doses >= 10 mg/kg/day and in females at 50 mg/kg/day; however, systemic toxicity was not observed. Consequently, the no-observed-adverse-effect level (NOAEL) for IBP was determined to be 50 mg/kg/day in rats of both sexes, indicating no impact on the endocrine system. The toxicokinetics of IBP exhibited dose-dependent systemic exposure, reaching a maximum dose of 50 mg/kg/day, and repeated administration over 13 weeks showed no signs of accumulation. https://doi.org/10.1007/s00204-024-03741-2

Single and combined exposures to bisphenol A and benzophenone-3 during early mouse pregnancy have differential effects on fetal and placental development,
FISCHER F., T. KRETSCHMER, P. SEIFERT, J. HOWANSKI, E. KRIEGER, J. RO, B. FINK, Z. R. YIN, M. BAUER, M. L. ZENCLUSSEN, N. MEYER, A. SCHUMACHER and A. C. ZENCLUSSEN, *Science of the Total Environment* 922 (Apr 2024),
Endocrine disrupting chemicals (EDCs) possess the capability to interfere with the endocrine system by binding to hormone receptors, for example on immune cells. Specific effects have already been described for individual substances, but the impact of exposure to chemical mixtures during pregnancy on maternal immune regulation, placentation and fetal development is not known. In this study, we aimed to investigate the combined effects of two widespread EDCs, bisphenol A (BPA) and benzophenone-3 (BP-3), at allowed concentrations on crucial pregnancy processes such as implantation, placentation, uterine immune cell populations and fetal growth. From gestation day (gd) 0 to gd10, female mice were exposed to 4 mu g/kg/d BPA, 50 mg/kg/d BP-3 or a BPA/BP-3 mixture. High frequency ultrasound and Doppler measurements were used to determine intrauterine fetal development and hemodynamic parameters. Furthermore, uterine spiral artery remodeling and placental mRNA expression were studied via histology and CHIP-RT-PCR,

respectively. Effects of EDC exposure on multiple uterine immune cell populations were investigated using flow cytometry. We found that exposure to BP -3 caused intrauterine growth restriction in offspring at gd14, while BPA and BPA/BP-3 mixture caused varying effects. Moreover, placental morphology at gd12 and placental efficiency at gd14 were altered upon BP -3 exposure. Placental gene transcription was altered particularly in female offspring after in utero exposure to BP -3. Flow cytometry analyses revealed an increase in uterine T cells and NK cells in BPA and BPA/BP-3-treated dams at gd14. Doppler measurements revealed no effect on uterine hemodynamic parameters and spiral artery remod- eling was not affected following EDC exposure. Our results provide evidence that exposure to BPA and BP -3 during early gestation affects fetal development in a sex -dependent manner, placental function and immune cell frequencies at the feto-maternal interface. These results call for inclusion of studies addressing pregnancy in the risk assessment of environmental chemicals. https://doi.org/10.1016/j.scitotenv.2024.171386

Subacute cadmium exposure changes different metabolic functions, leading to type 1 and 2 diabetes mellitus features in female rats,
DA COSTA C. S., T. F. DE OLIVEIRA, F. C. F. DOS SANTOS, A. S. PADILHA, M. KRAUSE, M. CARNEIRO, L. MIRANDA-ALVES and J. B. GRACELI, *Environmental Toxicology* (2024 May 2024),
Cadmium (Cd) is a heavy metal that acts as endocrine disrupting chemical (EDC). Few studies have investigated the effects of Cd exposure on metabolic dysfunctions, such as type 1 and 2 diabetes mellitus (T1DM and T2DM). Thus, we assessed whether subacute Cd exposure at occupational levels causes abnormalities in white adipose tissue (WAT), liver, pancreas, and skeletal muscle. We administered cadmium chloride (CdCl2) (100 ppm in drinking water for 30 days) to female rats and evaluated Cd levels in serum and metabolic organs, morphophysiology, inflammation, oxidative stress, fibrosis, and gene expression. High Cd levels were found in serum, WAT, liver, pancreas, and skeletal muscle. Cd-exposed rats showed low adiposity, dyslipidemia, insulin resistance, systemic inflammation, and oxidative stress compared to controls. Cd exposure reduced adipocyte size, hyperleptinemia, increased cholesterol levels, inflammation, apoptosis and fibrosis in WAT. Cd-exposed rats had increased liver cholesterol levels, insulin receptor beta (IR beta) and peroxisome proliferator-activated receptor-gamma coactivator-1alpha (PGC1 alpha) expression, karyomegaly, inflammation, and fibrosis. Cd exposure reduced insulin levels and pancreatic islet size and increased inflammation and fibrosis. Cd exposure reduced skeletal muscle fiber diameter and increased IR expression and inflammation. Finally, strong positive correlations were observed between serum, tissue Cd levels, abnormal morphology, tissue inflammation and fibrosis. Thus, these data suggest that subacute Cd exposure impairs WAT, liver, pancreas and skeletal muscle function, leading to T1DM and T2DM features and other complications in female rats.
https://doi.org/10.1002/tox.24306

Transcriptome analysis during 4-vinylcyclohexene diepoxide exposure-induced premature ovarian insufficiency in mice,
LI Y., R. F. HE, X. QIN, Q. Y. ZHU, L. J. MA and X. L. LIANG, *Peerj* 12 (Apr 2024),
The occupational chemical 4-Vinylcyclohexene diepoxide (VCD) is a reproductively toxic environmental pollutant that causes follicular failure, leading to premature ovarian insufficiency (POI), which significantly impacts a woman's physical health and fertility. Investigating VCD's pathogenic mechanisms can offer insights for the prevention of ovarian impairment and the treatment of POI. This study established a mouse model of POI through intraperitoneal injection of VCD into female C57BL/6 mice for 15 days. The results were then compared with those of the control group, including a comparison of phenotypic characteristics and transcriptome differences, at two time points: day 15 and day 30. Through a comprehensive analysis of differentially expressed genes (DEGs), key genes were identified and validated some using RT-PCR. The results revealed significant impacts on sex hormone levels, follicle number, and the estrous cycle in VCD-

induced POI mice on both day 15 and day 30. The DEGs and enrichment results obtained on day 15 were not as significant as those obtained on day 30. The results of this study provide a preliminary indication that steroid hormone synthesis, DNA damage repair, and impaired oocyte mitosis are pivotal in VCDmediated ovarian dysfunction. This dysfunction may have been caused by VCD damage to the primordial follicular pool, impairing follicular development and aggravating ovarian damage over time, making it gradually difficult for the ovaries to perform their normal functions. https://doi.org/10.7717/peerj.17251