Bulletin de veille Perturbateurs Endocriniens N°32 – Octobre 2025

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.

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Exposition professionnelle

Multiple maternal occupational exposures during pregnancy and intrauterine growth: analysis of the French Longitudinal Study of Children - ELFE cohort, using data-driven approaches.
Tartaglia M, Ge C, Pronk A, Costet N, Audignon-Durand S, Houot MT, et al. *Int J Hyg Environ Health*. 2025 Sep 5;270:114666.
OBJECTIVE: To use data-driven approaches to investigate maternal multi-occupational exposures during pregnancy and their effects on intrauterine growth. METHODS: Maternal occupational exposure to 47 factors during pregnancy was evaluated with job-exposure matrices in the French ELFE

cohort. The outcomes of interest were birthweight (BW), small for gestational age (SGA) and head circumference (HC). Occupational exposures associated with these outcomes were identified by EWAS, LASSO, and random forest. The five exposures with the strongest effects selected with these approaches were included in a final multivariate model with significant interactions. RESULTS: We included 12,851 women. The most important occupational factors predictive of SGA were endocrine disruptors, high strain, kneeling/squatting, job demands, physical effort. No significant associations were detected when these variables were combined in a final model. For BW, the most important variables were leaning forward/sideways, using a computer screen, ultrafine particles, physical effort, airborne germs, repetitive actions. The use of a computer screen significantly decreased BW and, for women not exposed to airborne germs, leaning forward/sideways significantly increased BW. For HC, repetitive actions, oxygenated solvents, kneeling/squatting, airborne germs, working outdoors were the most important predictive factors. Repetitive actions and working outdoors significantly decreased HC. HC also decreased in women exposed to both airborne germs, and oxygenated solvents. Similar results were found for women who worked during the third trimester. CONCLUSION: Our findings highlight potential roles of chemical, biological and postural factors and their interactions in determining intrauterine growth. These results highlight the importance of considering multiple exposures in occupational health studies.

Lien vers l'article

Phthalate exposure is associated with subclinical coronary atherosclerosis: The Aragon Workers' Health Study (AWHS).

Mérida DM, Torrijo-Belanche C, Moreno-Franco B, Laclaustra M, Rey-García J, Gimeno-Ruiz S, et al. *Am J Prev Cardiol*. 2025 Sep;23:101072.

BACKGROUND AND OBJECTIVES: Phthalates are implicated in mechanisms underlying the development of cardiovascular disease, such as oxidative stress, lipid peroxidation, endothelial dysfunction, and activation of procoagulant pathways. This study aimed to evaluate the association between phthalate exposure and subclinical coronary atherosclerosis (SCA). METHODS: A total of 1119 Spanish male workers from a car assembly plant (mean age: 50.9 years) were included. Urinary metabolites of 11 phthalates and ΣDEHP were analyzed. SCA was defined as coronary artery calcium ≥ 100 Agatston units. Logistic regression models were used to estimate the association between phthalates (natural log-transformed) and SCA, adjusting for sociodemographic, lifestyle, and cardiovascular risk factors. Dose-response relationships were explored using restricted cubic splines. RESULTS: The prevalence of SCA was 10.2 %. Participants with SCA had a median Mono-ethyl phthalate (MEP) concentration of 126.1 µg/g-creatinine compared to 99.3 µg/g-creatinine in those without SCA. A 1-unit increase in the natural logarithm of MEP was associated with a 21 % higher prevalence of SCA (OR: 1.21; 95 % CI: 1.02-1.44), showing a linear relationship. Positive but non-significant associations were observed for MiBP and MnBP. Sensitivity analyses with phthalates in original units (ng/ml) and adjustments for urinary creatinine showed consistent results. CONCLUSIONS: Exposure to MEP is associated with an increased prevalence of SCA in male workers, suggesting that the exposure to this phthalate may play a role in the early stages of cardiovascular disease. These findings provide a basis for public health initiatives aimed at reducing phthalate exposure for the primary prevention of cardiovascular disease.

Lien vers l'article

The effects of parental occupational exposures on autism spectrum disorder severity and skills in cognitive and adaptive domains in children with autism spectrum disorder.

McCanlies EC, Gu JK, Ma CC, Sanderson WT, Ludeña-Rodriguez YJ, Hertz-Picciotto I. *Int J Hyg Environ Health*. 2025 Jul;268:114613.

Lien vers l'article

Occupational Exposure to Engine Exhausts and Prostate Cancer Risk,
Barul, C., Rousseau, M. C. and Parent, M. E., *Environmental Health*, Jul 25 2025, Vol. 24, no. 1.

Background Some engine exhausts (EEs) have been classified as carcinogens and/or can have hormone-modulating properties that could play a role in prostate cancer development.ObjectiveWe investigated associations between lifetime occupational exposure to various EEs and prostate cancer risk, overall and for aggressive cancers.MethodsIn a population-based case-control study conducted in Montreal, Canada, 1,924 incident histologically-confirmed prostate cancer cases (436 aggressive) and 1,989 population controls were recruited. Socio-demographics, lifestyle factors and a detailed occupational history were collected during in-person interviews. Industrial hygienists conducted evaluations of intensity, frequency and reliability of exposure to EEs resulting from the combustion of several fuels (any diesel, light- and heavy-duty diesel, leaded and unleaded gasoline, propane and jet fuel) in each job held >= 2 years. Odds ratios (ORs) and 95% confidence intervals (CI) were estimated for exposure to each EE, in association with prostate cancer risk, adjusting for age and then for potential lifestyle and occupational confounders, accounting for a 5-year latency period. As most associations were not linear, we fitted functions for changes in percentile distributions based on natural cubic splines. Results There was no evidence of associations between exposure to the various EEs and overall prostate cancer. However, for high-grade cancers, based on the fully-adjusted model, a change from the 25th to the 75th percentile of the exposure distribution of any diesel EE yielded an OR of 1.24 (95%CI 0.96-1.61), and of 1.27 (95% CI 0.80-2.01) for a change from the 75th to the 95th percentile. These increases reflected exposure to diesel EE from light-duty vehicles, associated with similar ORs. For leaded gasoline EE, a change from the 75th to the 95th percentile resulted in an age-adjusted OR of 1.36 (95%CI 0.88-2.11), which was attenuated to 1.12 (95%CI 0.63-2.02) after full adjustment. There were no associations with EE from unleaded gasoline, diesel from heavy-duty vehicles, jet fuel and propane. Conclusion There was suggestive evidence for a deleterious role of occupational exposure to EE resulting from the combustion of any diesel, light-duty diesel and from leaded gasoline in the development of aggressive prostate cancer. Results were independent from prostate cancer screening patterns. https://doi.org/10.1186/s12940-025-01205-3

PFAS (substances per et polyfluorées) : définition, toxicité, exposition des pompiers,
Bonneterre, V. and Persoons, R., *Archives des Maladies Professionnelles et de l'Environnement*, 2025/10/01/ 2025, Vol. 86, no. 5, p. 102897.

Conclusion Les PFAS, doivent donc être abordés comme un sujet de santé-travail au même titre qu'ils sont nu sujet de santé environnement, et plus généralement un sujet une seule santé (impactant, au-delà de la santé humaine, la santé animale et celle des écosystèmes). Cela implique en premier lieu une identification de leur présence, la traçabilité des expositions et imprégnations (avec les challenges que cela suppose car tous ne sont pas dosables et l'interprétation demeur délicate) ainsi qu'un travail de substitution et de prévention des expositions. Les travailleurs, dans la mesure où ils sont plus exposés, pourraient être sentinelles d'effets sanitaires décrits ou à décrire. Les médecins du travail confrontés à ce sujet sont invités à se rapprocher des Centres régionaux de pathologies professionnelles et environnementales (CRPPEs). Il n'existe pas encore en France de recommandations particulières de suivi médical pour les exposés, tandis que de premières propositions commencent à être faites à l'international, comme aux USA [13]. La HAS, appuyée par la Société française de toxicologie clinique, devrait donc fournir des recommandations en ce sens en 2026. https://doi.org/10.1016/j.admp.2025.102897

A Scoping Review on Male-Mediated Developmental Toxicity,
Caporossi, L., Castellano, P., Paci, E. and Pigini, D., *Toxics*, Aug 22 2025, Vol. 13, no. 9.

Background: Developmental toxicity is defined as adverse effects induced either during pregnancy or as a result of parental exposure. While considerable attention has been devoted to maternal exposure to such chemicals, the role of paternal exposure has often been regarded as less significant. Objective: This study aims to highlight the impact of male-mediated developmental toxicity. Methods: An online search was conducted using PubMed, Scopus, and Google Scholar to identify studies focusing on developmental toxicity in offspring associated with paternal exposure during the preconception period. Results: The scientific literature-ranging from studies on pharmaceutical use to substances of abuse (notably tobacco, alcohol, opioids, and cannabinoids), as well as occupational and environmental exposure to specific compounds (e.g., phthalates, certain organic solvents, pesticides)-indicates that paternal exposure to developmental toxicants can adversely affect offspring health through various biochemical mechanisms. Conclusions: There is substantial experimental evidence of male-mediated developmental toxicity for various chemicals, demonstrating a particular vulnerability of the male germ line to transmissible effects. Several mechanisms have been proposed to explain the biochemical pathways underlying this toxicity. Evidence in humans is more challenging to interpret; however, numerous findings-both concerning substances of abuse and occupational exposures-raise concerns regarding the potential developmental risks to offspring. https://doi.org/10.3390/toxics13090707

Exposure to Lead Compounds in an Industrial Setting and the Effects on the Thyroid Gland: A Pilot Cohort Study,
Caporossi, L., Di Renzi, S., De Rosa, M., Capanna, S., Partenzi, E., D'alessandro, I. and Papaleo, B., *Hygiene*, Apr 3 2025, Vol. 5, no. 2.

Background: Lead compounds are chemicals of high toxicological concern and are suspected to interact with the thyroid axis. Method: A cohort study was carried out involving 70 workers from a petrochemical company exposed to inorganic lead compounds. All recruited workers were given a clinical anamnestic questionnaire aimed at characterizing their endocrine and thyroid status. A blood test was conducted to dose the amount of lead, thyroid hormones (FT3, FT4, TSH), and antibodies (TGAb and TPOAb). Samples were stratified according to working seniority and lead exposure levels. A regression study was conducted to highlight trends in hormones and antibodies versus lead levels. Results: Most of the dosages are within the normal ranges. The regression study showed how higher lead values are correlated with a reduction in TSH and an increase in FT3 and FT4. There is a statistically significant increase in TPOAb in the most exposed workers. Conclusions: The trends of thyroid hormones may suggest a tendency towards hyperthyroidism for higher lead exposure, while the increase in TPOAb could indicate a greater predisposition to the development of autoimmune thyroid diseases. https://doi.org/10.3390/hygiene5020013

Environmental and occupational risks to reproductive health in women service members and veterans,
Clark, K. L., *Frontiers in Public Health*, Aug 13 2025, Vol. 13.

Women have played a vital role in the U.S. military for decades, with their presence steadily increasing. However, despite this growth, research on the unique occupational and environmental exposures they face remains limited, highlighting the need for greater understanding to improve reproductive health outcomes. Chemical exposures such as burn pit emissions, airborne particulates, heavy metals, and pesticides can disrupt hormone regulation and pose risks for fertility, miscarriage, preterm birth, and congenital anomalies. Additional risks include unsafe water sources,

contaminated soil, increased vaccinations, and extreme environmental conditions. However, studies on these exposures remain inconsistent, with some indicating significant reproductive risks while others show minimal or no impact. This mini review highlights what is currently known about the impact of military-related environmental and occupational exposures on women's reproductive health and identifies key gaps in the literature. Further research is essential to determine high-risk exposures, guide policy development, and support early intervention strategies. Addressing the long-term impact of military-related environmental exposures is crucial for ensuring better health outcomes and facilitating access to care for female service members and veterans. https://doi.org/10.3389/fpubh.2025.1628858

Endocrine disruptors and male infertility: multi-omics identification of key genes in non-obstructive azoospermia,
Hong, Y. G., Wang, Y. R., Li, J. J., Shu, W. Y., Chen, H. L. and Chen, C. D., *Journal of Assisted Reproduction and Genetics*, 2025.

Purpose Environmental endocrine-disrupting chemicals (EDCs) are increasingly implicated in male infertility, yet the gene-level mechanisms by which EDCs contribute to non-obstructive azoospermia (NOA) remain unclear. This study aimed to identify EDC-related genes that are causally linked to NOA and uncover their potential roles in reproductive dysfunction. Methods We integrated transcriptomic analysis of GEO datasets, EDC-associated gene data from the Comparative Toxicogenomics Database (CTD), and Mendelian randomization (MR) to prioritize candidate genes with causal relevance to male infertility. Phenome-wide association study (PheWAS) was conducted to assess systemic effects. EDC-gene interactions were visualized, and single-cell RNA sequencing (scRNA-seq) was used to validate cell-type-specific gene expression in the testis. Results A total of 136 genes were identified at the intersection of differentially expressed genes in NOA and EDC-related genes. MR analysis highlighted PPP6R1 and AP1M2 as causally linked to male infertility. PheWAS revealed a significant association between PPP6R1 and cardiovascular traits ($p < 1 \times 10-6$), suggesting pleiotropic effects. Interaction analysis identified 26 EDCs targeting these genes, including thiram, bisphenol A, and sodium arsenite. The scRNA-seq confirmed downregulation of both genes in germ cells of NOA patients. Conclusion Our multi-omics approach suggests a potential EDC-gene-NOA axis, identifying PPP6R1 and AP1M2 as candidate genes whose expression may be influenced by environmental exposure in the context of male infertility. These findings deepen mechanistic understanding of NOA pathogenesis and support future research into environmental and molecular targets for diagnosis and prevention. https://doi.org/10.1007/s10815-025-03664-6

Breast cancer-related occupational exposures facing immigrant women,
Knox, K. E., Ohayon, J. L., Carrera, E., Rudel, R. A. and Morello-Frosch, R., *Journal of Exposure Science and Environmental Epidemiology*, 2025.

BackgroundImmigrants comprise roughly 14% of the U.S. population, and studies indicate that breast cancer increases among some immigrant groups after relocating to the U.S.ObjectiveWe characterized exposures to breast cancer-relevant chemicals in jobs commonly occupied by U.S. immigrant women, aged 18-65.MethodsWe analyzed data from the American Community Survey Public Use Microdata Sample to profile which occupations are most prevalent for immigrant women and integrated these results with data on occupational chemical exposures from the Women's Occupations and Risk from Chemicals tool, which identifies occupations with probable and possible chemical exposures of relevance for breast cancer.ResultsImmigrant women most commonly work as house cleaners, nurses, cashiers, janitors, and care aides, and comprise 71% of manicurists. We prioritize the occupations house cleaners and nurses for their combination of high potential exposures and the large number of immigrant women employed in these occupations. Chemicals of

interest are those found in fragrances, and cleaning and maintenance products, including phthalates, antimicrobials, and alkylphenols. Many of these compounds are mammary gland carcinogens and developmental toxicants, and/or endocrine disruptors.ImpactThere are few studies of breast cancer-relevant chemical exposures for most occupations, including those heavily represented by immigrant women. By identifying jobs that employ large numbers of immigrant women and are associated with a high likelihood of exposure to potential breast carcinogens, we inform future research on breast cancer-relevant exposures and opportunities for preventative exposure reduction. We also show that immigrant women with lower levels of education and English fluency work in occupations with more potential for harmful chemical exposures. https://doi.org/10.1038/s41370-025-00808-9

Circular RNA hsa_circ_0099188 regulates inducible nitric oxide synthase and chemokine transcription in macrophages by targeting the hsa-miR-381-3p/PPP3CA and hsa-miR-381-3p/KLF4 pathways in response to 4,4'-methylene diphenyl diisocyanate-glutathione conjugate exposure, Lin, C. C., Law, B. F. and Hettick, J. M., *Toxicological Sciences*, 2025.

Workplace exposure to 4,4 '-methylene diphenyl diisocyanate (MDI), the most used monomeric diisocyanate, can lead to the development of occupational asthma (OA). However, the molecular mechanisms by which MDI induces OA remain poorly understood. Previous studies have shown that exposure to MDI or MDI-glutathione (GSH) conjugate reduces the levels of endogenous human (hsa)/murine (mmu)-microRNA (miR)-206/381-3p, triggering the activation of calcineurin/nuclear factor of activated T-cells/inducible nitric oxide synthase (NOS2) regulatory axis and Kr & uuml;ppel-like factor 4 (KLF4)/chemokine pathways in macrophages. Circular RNAs (circRNAs) play important roles on miR and miR-mediated functions in the cells. CircRNA hsa_circ_0008726 is induced by MDI-GSH to downregulate endogenous hsa-miR-206-3p in macrophages; however, the MDI-GSH mediated circRNA response to downregulate hsa-miR-381-3p is currently unknown. The expression of previously identified candidate circRNAs that bind hsa-miR-381-3p were analyzed in differentiated/enhanced THP-1 macrophages treated with MDI-GSH conjugates using RT-qPCR. MDI-GSH exposure induces endogenous hsa_circ_0099188 and its host gene thyrotropin-releasing hormone-degrading ectoenzyme (TRHDE); however, other candidate circRNAs were neither detected nor altered. RNA immunoprecipitation experiments confirmed the binding of hsa-miR-381-3p to hsa_circ_0099188. Further experiments demonstrate that modulating hsa_circ_0099188 expression through siRNAs or overexpression plasmids alter the levels of endogenous hsa-miR-381-3p, PPP3CA, and KLF4, as well as NOS2 and M2 macrophage-associated markers and chemokine transcripts. These findings suggest that MDI/MDI-GSH exposure leads to the downregulation of hsa-miR-381-3p by inducing the expression of hsa_circ_0099188/TRHDE, thereby enhancing the regulatory effects of hsa-miR-381-3p in macrophages. https://doi.org/10.1093/toxsci/kfaf114

Epidémiologie

Longitudinal analysis of maternal exposure to phthalates and bisphenol A and their impact on infant neurodevelopment and autistic behavior: The potential mediating role of thyroid hormones,
Al-Saleh, I., Aljerayed, Y., Gheith, M., Alobaid, N., Alenazi, H., Elkhatib, R., Aldhalaan, H., Alnemer, M., Mohamed, G. and Shoukri, M., *International Journal of Hygiene and Environmental Health*, Aug 2025, Vol. 269.

This prospective cohort study investigated the impact of maternal exposure to endocrine-disrupting chemicals, specifically phthalates and bisphenol A (BPA), on infant neurodevelopment. From 2019 to 2022, 672 pregnant women consented to participate in the study during their initial prenatal appointments at the Obstetrics and Gynecology Clinic of King Faisal Specialist Hospital & Research Centre. Two urine samples were collected each trimester to measure seven phthalate metabolites and BPA levels. Neurodevelopmental performance was evaluated using the Ages & Stages Questionnaires (R) Third Edition at 6, 12, and 18 months of age, and the risk of autism was assessed with the Modified Checklist For Autism in Toddlers at 18 months. Linear mixed models and logistic regression were applied to evaluate trimester-specific and overall associations using natural log-transformed urinary concentrations of phthalates and BPA. Our results showed that each one-unit increase in the log-transformed concentration of specific phthalates and BPA was associated with significant changes in infant developmental scores. During the first trimester, elevated levels of mono-n-butyl phthalate (MnBP), monoiso-butyl phthalate (MiBP), and BPA were associated with 4.3 %-5.6 % decreases in gross motor (GM) scores. In contrast, monoethyl phthalate (MEP) and low-molecular-weight (& sum;LMW) phthalates were linked to 4 %-4.5 % increases in communication (COMM) scores. In the third trimester, MECPP and Sigma 3DEHP were positively associated with GM and fine motor (FM) scores, while MiBP was associated with reduced personal-social (PSoc) scores. Sex-stratified analyses revealed differences in susceptibility, with males showing stronger adverse associations in problem-solving and social domains and females more affected in gross and fine motor scores. Mediation analysis identified free thyroxine (FT4) as a partial mediator, accounting for 12.7 % of the effect of & sum;LMW phthalates on COMM scores during the first trimester. However, most mediation effects through maternal thyroid hormones were small and not statistically significant. Additionally, some first-trimester exposures, such as MEP and mono-(2-ethyl-5-oxohexyl) phthalate, appeared to be associated with lower odds of a positive M-CHAT screen. At the same time, MnBP showed a potential increase in risk. However, these exploratory findings were based on crude models and a limited number of positive cases and should be interpreted cautiously. Our study also examined overall exposure to phthalates and BPA across pregnancy, revealing consistent yet subtle impacts across developmental domains. This study adds novel insights by assessing trimester-specific exposures and investigating maternal thyroid hormones as potential mediators of early neurodevelopmental outcomes.
https://doi.org/10.1016/j.ijheh.2025.114647

Role of phthalates in breast cancer initiation, progression and drug rersistance: A scoping review and recommendations,
Benoit, L., Tomkiewicz, C., Bortoli, S., Bats, A. S., Coumoul, X. and Koual, M., *Toxicology Letters*, Nov 2025, Vol. 413.

Phthalates are endocrine-disrupting chemicals (EDCs) with implications in breast cancer (BC). This review synthesizes epidemiological and experimental data to evaluate the role of phthalates in BC initiation, progression, and therapeutic resistance. We performed a scoping review using bibliographic citations from PubMed, Clinical Trials.gov, Embase, Cochrane Library, and Web of Science databases. MeSH terms for breast cancer and phthalates were combined and not restricted to the English language. The search was performed from 2010 to July 2024. The primary outcome was to determine the role of phthalates in BC. Two hundred and forty-seven articles were screened from 2010 to 2024. Of the 90 studies included, 23 were reviews, 24 were epidemiologic and 43 were experimental. Epidemiological evidence is mixed, with certain studies identifying a correlation between high cumulative exposure to specific phthalates, such as dibutyl phthalate, and increased BC risk, particularly in estrogen receptor-positive subtypes. Conversely, other studies reported no significant associations. Experimental investigations have demonstrated that phthalates disrupt estrogenic signaling, induce BC cell proliferation, and potentiate metastasis. Additionally,

phthalates contribute to chemoresistance by modulating drug metabolism and altering gene expression. Given the persistent exposure to phthalates this review calls for public health interventions and recommendations. https://doi.org/10.1016/j.toxlet.2025.111721

Maternal phthalate exposure, gestational length, and preterm birth risk: a prospective cohort study nested within a randomised trial,
Best, K. P., Yelland, L. N., Ge, L., Shi, Z. M., Leemaqz, S., Gibson, R., Makrides, M. and Middleton, P., *Bmc Pregnancy and Childbirth*, Aug 8 2025, Vol. 25, no. 1.

Background Preterm birth (< 37 weeks gestation) is a leading cause of infant morbidity and mortality, yet the underlying causes remain unknown in many cases. Environmental exposures, including endocrine-disrupting chemicals such as phthalates, have been implicated in preterm birth risk. Phthalates are commonly used as plasticisers in consumer products, resulting in widespread human exposure. While some studies suggest an association between maternal phthalate exposure and reduced gestational length, findings remain inconsistent. This study aimed to investigate the relationship between urinary phthalate metabolite concentrations and gestational length in an Australian pregnancy cohort. Methods This prospective cohort study was nested within the Omega-3 to Reduce the Incidence of Prematurity (ORIP) trial. A total of 605 women with singleton pregnancies from South Australia provided urine samples between 22- and 26-weeks' gestation for phthalate metabolite analysis. Thirteen phthalate metabolites were quantified using liquid chromatography-tandem mass spectrometry. Gestational age at birth was determined from medical records. Linear regression models assessed associations between phthalate concentrations and gestational length, adjusting for maternal characteristics including age, BMI, socioeconomic status, education, smoking, and alcohol consumption. Results Phthalate metabolites were detected in > 99% of urine samples, with the highest concentrations observed for mono-ethyl phthalate (MEP), mono-isobutyl phthalate (MiBP), and mono-butyl phthalate (MBP). There was no evidence of an association between phthalate exposure and gestational length in either unadjusted or adjusted analyses. No significant association was found between phthalate exposure and preterm birth risk. Conclusions Despite widespread phthalate exposure, no clear link was identified between maternal phthalate levels and shortened gestation in this Australian cohort. However, continued surveillance is needed to monitor emerging plasticiser exposures and inform public health policies on maternal and infant health. https://doi.org/10.1186/s12884-025-07980-8

Associations Between Prenatal Phthalate Exposure and Atopic Symptoms in Childhood: Effect Modification by Child Sex,
Bhatt, K. D., Mistry, S., Lamadrid-Figueroa, H., Tamayo-Ortiz, M., Mercado-Garcia, A., Lane, J. M., Tellez-Rojo, M. M., Wright, R. O., Wright, R. J., Estrada-Gutierrez, G., Carroll, K. N., Alcala, C. S. and Rosa, M. J., *Toxics*, Sep 3 2025, Vol. 13, no. 9.

Background: The global rise in atopic diseases, like atopic dermatitis and allergic rhinitis, may be linked to prenatal exposure to endocrine-disrupting chemicals like phthalates, with potential sex-specific effects. Methods: We analyzed 558 mother-child pairs from the PROGRESS birth cohort in Mexico City. Maternal urinary phthalate metabolites were measured during the 2nd and 3rd trimesters. Atopic dermatitis and allergic rhinitis symptoms were assessed at ages 4-6 and 6-8 years using the International Study of Asthma and Allergies in Childhood survey. Weighted Quantile Sum Regression (WQS) was used to assess sex-specific mixture associations. Individual sex-specific phthalate associations were examined using modified Poisson models with inclusion of product terms and stratification. Models were adjusted for maternal age, education, parity, pre-pregnancy body mass index, and prenatal tobacco exposure. Results: We found that child sex modified associations between the 2nd trimester phthalate mixture and current atopic dermatitis symptoms

*at both 4-6 years (WQS*sex OR: 1.23, 95% CI: 1.00-1.60) and 6-8 years (WQS*sex OR: 1.46, 95% CI: 1.01-2.10). Among males, higher phthalate concentrations were positively associated with symptoms at both ages (OR: 1.10, 95% CI: 0.92, 1.32; OR: 1.16, 95% CI: 0.92, 1.46), while associations were negative in females (OR: 0.87, 95% CI: 0.73, 1.04; OR: 0.79, 95% CI: 0.62, 1.02). No sex-specific associations were found for 3rd trimester exposures. Individual metabolite analyses also showed effect modification by sex for 2nd trimester exposures. Conclusions: Prenatal exposure to phthalates is associated with atopic dermatitis symptoms in childhood in a sex-specific manner.* https://doi.org/10.3390/toxics13090749

Integrated network toxicology and population-based analysis uncovers organophosphate flame retardant exposure as a risk factor for hepatic steatosis and fibrosis: mechanistic and clinical insights,
Che, L., Jiang, R. J., Wang, C. Q., He, J. L., Zhang, Z. Y. and Qian, B., *International Journal of Surgery*, Sep 2025, Vol. 111, no. 9, p. 6036-6049.

Background:Laboratory evidence has recently shown that exposure to organophosphate flame retardants (OPFRs) can cause adverse liver outcomes, which lacks further validation.Objective:This investigated the correlation and toxicological mechanism between OPFRs exposure and hepatic steatosis or fibrosis.Method:To explore the association of OPFRs exposure and hepatic steatosis or liver fibrosis, we conducted the population analysis using the data of urinary OPFRs monitoring and liver vibration-controlled transient elastography examinations from the National Health and Nutrition Examination Survey during 2017-2018. Network toxicology and transcriptomics analyses were used to explore the potential toxicological mechanisms of OPFRs-associated hepatic steatosis.Results:Univariate analysis suggested that urinary bis(1,3-dichloro-2-propyl) phosphate level was negatively correlated with the risk of hepatic steatosis. Nonlinear relationships were observed between urinary diphenyl phosphate levels and the risk of hepatic steatosis in restricted cubic splines analysis. Network toxicology and transcriptomics analysis suggested that OPFRs might directly interact with several metabolism-related proteins, including monoglyceride lipase, fatty acid amide hydrolase, cannabinoid receptor 1 (CNR1), CNR2, and phosphatidylinositol-5-phosphate 4-kinase type 2 gamma (PIP4K2C). These interactions could disrupt lipid metabolic processes by altering lipid metabolism (e.g. PPAR signaling pathway and insulin signaling pathway), energy metabolism (e.g. adipocytokine signaling pathway and HIF-1 signaling pathway), and apoptosis pathway (e.g. p53 signaling pathway), thereby contributing to hepatic steatosis.Conclusion:Our results indicate that OPFRs exposure was associated with adverse pathological changes in the liver. https://doi.org/10.1097/js9.0000000000002680

The effect of phytoestrogens and PAHs on endometriosis and the involvement of gut microbiota, inflammation, and molecular targets,
Chen, Y. L., Jiang, Y. T., Li, Z. Y., Zhu, M. Y., Akimana, A. G., Wang, K., Zhou, K., Zhang, X. L., Ji, X. M. and Chen, M. J., *Scientific Reports*, Oct 15 2025, Vol. 15, no. 1.

Endometriosis is a common estrogen-dependent inflammatory disease, yet its complex etiology is not fully understood. Endocrine Disrupting Chemicals (EDCs) exposure disrupts human reproduction, but studies on mixed EDCs and endometriosis risk are Limited. The study Analyzed 2,644 women, assessing 12 phthalates, 8 polycyclic aromatic hydrocarbons, And 6 phytoestrogens in a representative US population. Various statistical models (generalized linear model, partial least squares discriminant analysis, weighted quantile sum, quantile g-computation, restricted cubic spline) were used to explore the link between EDC exposure and endometriosis risk, with mediating effects of lipid metabolism and inflammatory biomarkers examined. Biological mechanisms were identified through an integrated strategy involving target analysis of key chemicals and

endometriosis intersections, network establishment, pathway analysis, and target validation. Various statistical models revealed that the gut microbiota metabolite enterolactone (ENL) was negatively associated with endometriosis, while the PAH metabolite 1-Hydroxyphenanthrene (1-OHPHE) was positively associated. Mediation analysis showed that uric acid (UA) and ferritin (Fer) were associated with mediating pathways in the relationships between ENL And decreased risk, And 1-OHPHE and increased risk, respectively. Network and target analysis indicated that ENL affects risk via ESR1, while 1-OHPHE disturbs it through GRB2. ENL can bind to XDH, inhibiting UA production. ENL supplementation may mitigate PAH-induced risks through the PI3K-Akt pathway. In conclusion, higher ENL levels were associated with reduced endometriosis risk, while 1-OHPHE was associated with increased prevalence. Inflammatory mediators UA And Fer demonstrated potential mediating associations in these relationships. ENL levels may be associated with attenuation of 1-OHPHE associations with endometriosis, potentially through gut microbiota-related pathways. These findings emphasize the role of environmental and microbiome interactions in modulating endometriosis risk. https://doi.org/10.1038/s41598-025-20042-5

Prenatal and early childhood exposure to phthalates and neurodevelopment in 42 months old children,
Cohen-Eliraz, L., Ornoy, A., Ein-Mor, E., Bar-Nitsan, M., Calderon-Margalit, R. and Pilowsky-Peleg, T., *Neurotoxicology*, Sep 2025, Vol. 110, p. 74-84.

Background: Increased prevalence of neurodevelopmental syndromes raises concerns regarding risks from environmental exposures. Phthalates are a class of chemicals widely used in daily products. It has been suggested that prenatal and early childhood exposure to phthalates are associated with disruption of developmental outcomes, cognitive and psychomotor functions. Aims: To estimate the association between prenatal and early childhood exposure to phthalates and neurodevelopmental outcomes. Methods: Women were recruited at 11-18 weeks of gestation and provided spot urine samples, analyzed for phthalate metabolites (DEHP, DiNP, MBzBP). Children (n = 102) were examined at 42 months of age, using a broad developmental assessment and standard maternal reports, regarding cognitive, developmental and behavioral problems (WPPSI-III, NIH-toolbox, NEPSY-II, CBCL, ASQ-3 questionnaires), and provided spot urine samples (n = 47). To explore the associations between tertiles or continuous levels of metabolites and developmental outcomes, multivariate general linear models (GLM) were used. Results: DEHP and DiNP metabolites were above the level of detection (>LOD) in more than 97 % of maternal specimens and MBzBP was detected in 88 % of maternal specimens. Increased DEHP levels were associated with problem solving scores among boys (scores: 53.24 + 2.34, 54.29 + 2.45, and 43.54 + 3.26 for low, medium and high DEHP tertiles, respectively; p = 0.029), and fine motor problems (47.58 + 2.93, 49.75 + 3.07, and 32.01 + 4.07 for low, medium and high DEHP tertiles, respectively; p = 0.003) and attention problems among girls (Flanker scores: 112.53 + 14.28, 110.3 + 12.93, and 98.83 + 12.65 for low, medium and high DEHP tertiles, respectively; p = 0.007). Moreover, in girls, a potential U-shaped association was found between levels of exposure to MBzBP and problem solving (54.55 + 6.87, 44.69 + 14.88, and 54.62 + 6.60 for low, medium and high MBzBP tertiles, respectively; p = 0.015), fine motor problems (56.36 + 5.04, 42.50 + 15.49, and 51.92 + 8.04 for low, medium and high MBzBP tertiles, respectively; p = 0.007), and verbal abilities (Vocabulary scores: 11.46 + 3.01, 8.25 + 3.43, and 11.53 + 2.69 for low, medium and high MBzBP tertiles, respectively; p = 0.007). Early childhood exposure was associated with fine motor scores and DEHP and MBzBP postnatal exposure (DEHP: beta = -0.010, Cl: -0.016, -0.004, p = 0.003; MBzBP: beta = -0.321, Cl: -0.499, -0.144, p = 0.001). Most associations became nonsignificant after FDR correction for multiple comparisons. Conclusion: This study suggests associations between prenatal exposure to phthalates and early childhood motor and cognitive abilities, with sex differences, and an association between

early childhood exposure with motor abilities. Larger studies are needed to confirm these exploratory findings. https://doi.org/10.1016/j.neuro.2025.07.007

A scoping review of the role of heritability and environmental exposures in the development and severity of benign prostatic hyperplasia,
Daryabari, S. S., Fendereski, K., Grimes, M. D., Gross, K. X., Summers, S., Ramsay, J. M. and Myers, J. B., *Translational Andrology and Urology*, Aug 2025, Vol. 14, no. 8, p. 2439-2455.

Background: Benign prostatic hyperplasia (BPH) is a common condition among aging men, significantly affecting quality of life and contributing to a substantial healthcare burden. The pathogenesis of BPH is strongly influenced by genetic factors, with heritability estimates showing a wide range from 20% to 83%. Emerging evidence also highlights the critical role of environmental exposures, including endocrine-disrupting chemicals (EDCs), in BPH risk, progression, and therapeutic response. This review synthesizes current knowledge on genetic and environmental determinants of BPH pathogenesis, severity, and management. Methods: A scoping review of the literature was conducted using the databases PubMed, Scopus, and Web of Science. Relevant studies on genetic predisposition, environmental exposures, and their contributions to BPH were analyzed. Data from epidemiological studies, genome-wide association studies (GWAS), familial aggregation analyses, and research on environmental exposures were integrated to provide an understanding of these factors and BPH pathogenesis. Results: Familial clustering indicates a significantly elevated risk, particularly among first-degree male relatives. Key genetic determinants include androgen receptor (AR) gene CAG repeat polymorphisms, where shorter repeats are linked to increased AR activity and prostate enlargement. Estrogen pathway genes, such as ESR1 and CYP19A1, and variants in dihydrotestosterone (DHT) synthesis genes, notably SRD5A2, influence disease progression and risk. GWAS have identified additional loci, such as MSMB and TERT, associated with prostate volume and aggressive BPH phenotypes. Polygenic risk scores offer promising applications in identifying individuals at high risk for severe BPH. Environmental exposures, particularly to EDCs such as bisphenol A (BPA), bisphenol S (BPS), and bisphenol AF (BPAF), were found to disrupt hormonal regulation, contributing to prostatic hyperplasia. Air pollution, primarily particulate matter, exacerbates prostate inflammation and hyperplasia, with regional differences in BPH symptom severity correlating with air quality. Lifestyle factors, including high-fat diets and sedentary behaviors, further modulate disease severity. Conclusions: The development and progression of BPH are shaped by a complex interplay of genetic and environmental factors. EDCs contribute significantly to prostatic hyperplasia, while heritable factors influence disease onset, severity, and response to treatment. Integrating genetic risk profiling and environmental exposure assessments into clinical practice holds the potential to enhance BPH management and personalized therapeutic strategies. https://doi.org/10.21037/tau-2025-342

Prenatal exposure to bisphenol-A and neurocognitive changes in children aged 2 to 5 years: a systematic review,
De Oliveira, I. V. M., De Albuquerque, F. M., Fernandes, A. D., Zanella, P. B. and Silva, M. A., *Reviews on Environmental Health*, 2025.

Bisphenol-A (BPA) is a synthetic organic compound considered an endocrine disruptor. Childhood exposure to BPA has been linked to impaired memory and learning, as well as Attention Deficit Hyperactivity Disorder. The aim of this study was to review the available literature on prenatal exposure to BPA and its relationship to the neurocognitive development of children aged 2-5 years. This systematic review (CRD42023494940 registration PROSPERO) was conducted between December 2023 and May 2024, following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guidelines. The Web of Science, Embase, and

PubMed databases were used for the search, with no publication date limit. The following terms, with the respective Boolean operators, were searched: ((bisphenol A) OR (BPA)) AND ((pregnancy) OR (pregnant woman)). Twenty-one longitudinal studies were selected for this review. Most studies have demonstrated negative effects of prenatal BPA exposure on the neurocognitive development of children aged 2-5 years. These results differed between the sexes, with females having lower emotional control, reduced language dominance and problem solving, and males having lower psychomotor development and higher prosocial behavior, among other differences. Overall, BPA exposure during pregnancy has been associated with hyperactivity, aggression, anxiety, depression, inattention, and sleep problems. It is concluded that maternal exposure to BPA during pregnancy results in adverse health effects in children aged 2-5 years, with impairments in their neurocognitive development. https://doi.org/10.1515/reveh-2024-0161

Breast milk bisphenol concentrations in Canada and South Africa and associations with body size among South African infants,
Elsiwi, B., Bayen, S., Chi, Z. H., Goodyer, C. G., Hales, B. F., Robaire, B., Bornman, R., Obida, M., Moodie, E. E. M. and Chevrier, J., *Environmental Research*, Nov 15 2025, Vol. 285.

Objective: Infants may be exposed to bisphenols (BP) via breastfeeding. These chemicals are known endocrine disruptors and may interfere with infant growth. However, their presence in breast milk and their associations with infant size remain unexplored in South Africa, where infants may be especially vulnerable to toxic effects. Methods: We measured BPA, BPS, and BPAF in breast milk samples obtained 4-8 weeks postpartum from mothers residing in rural (Vhembe district; n = 193) and urban (Pretoria; n = 189) areas of South Africa and compared them to samples from Montreal, Canada (n = 206). Infant length and head circumference were measured in South Africa, with z-scores computed based on World Health Organization (WHO) growth charts. Random forest plots were used to identify top-ranked BP predictors, and linear marginal structural models were used to estimate associations between BP concentrations and infant size. Results: BP concentrations were highest in Vhembe relative to Pretoria; in Montreal, only BPS was detected. Microwaving food in plastic containers and maternal diet were important determinants of exposure. In the combined South African sites, total BPAF detection was associated with greater infant length ((3 = 0.38 SD, 95 % CI: 0.09, 0.68) and head circumference ((3 = 0.52 SD, 95 % CI: 0.23, 0.81). Associations were strongest in Pretoria. In contrast, a tenfold increase in total BPA concentration was associated with a 0.20 SD decrease in head circumference (95 % CI:-0.39,-0.01) in Vhembe. Conclusion: Findings point to high BP exposure in rural Africa and suggest that exposure to BPA and BPAF may be related to altered growth among South African infants. https://doi.org/10.1016/j.envres.2025.122452

Human liver perfluorooctane sulfonate associates with steatotic liver disease in a sex-dependent manner,
Flam, E., Lienard, V., Raverdy, V., Derhourhi, M., Froguel, P., Bonnefond, A., Lefebvre, P., Pattou, F., Eberle, D., Haas, J. T. and Staels, B., *Environment International*, Oct 2025, Vol. 204.

Perfluorooctane sulfonate (PFOS) is a persistent and widespread contaminant found in the environment and, as a consequence, in the human body, and is linked to adverse health effects, including steatotic liver disease (SLD). Human studies on the role of PFOS in SLD have been largely epidemiological, relying on plasma without measuring liver PFOS. However, using plasma PFOS levels to evaluate fatty liver disease is not comprehensive, and the effects of PFOS in human liver have not been described. We investigated the association of PFOS in plasma (P-PFOS) and liver (L-PFOS) with clinical parameters of Metabolic dysfunction-Associated SLD (MASLD) in a large human cohort with obesity and histology-confirmed MASLD. Combining liver RNA-seq and metabolomic data from liver and plasma, we correlated L- and P-PFOS with mRNA transcripts and metabolites to

identify dysregulated transcriptional and metabolic pathways. In women, L-PFOS negatively correlated with MASLD prevalence and severity. Conversely, in men, P-PFOS and L-PFOS positively associated with fibrosis. LPFOS quartile analysis showed potential threshold effects in several histological parameters in men only. In women, L-PFOS negatively correlated with metabolites from pathways implicated in MASLD progression, including diacylglycerol and sphingolipid species. At the gene expression level, L-PFOS correlated negatively with many fibrosis-related genes involved in collagen formation and extracellular matrix organization in women only. Generally, L-PFOS correlated with many disease-relevant variables in women, but with few in men. These correlations in women were opposite the clinical and molecular changes seen in MASLD progression, while the positive correlation between L-PFOS and liver fibrosis in men suggests a positive relationship with liver disease. https://doi.org/10.1016/j.envint.2025.109838

The link between prenatal exposure to a chemical mixture, cord blood hormones, and birth weight: an epidemiologic study,
Govarts, E., Cox, B., Portengen, L., Rodriguez-Carrillo, A., Carsique, M., Covaci, A., Den Hond, E., De Henauw, S., Nawrot, T., Leermakers, M., Patteet, L., Schettgen, T., Crepet, A., Van Klaveren, J., Vermeulen, R. and Schoeters, G., *Environment International*, Aug 2025, Vol. 202.

Prenatal chemical exposure has frequently been associated with fetal growth, although the underlying molecular mechanisms remain unclear. This study aims to explore the potential mediating role of hormones in the association between prenatal chemical mixture exposure and birth weight. We used data of 432 newborns from two Flemish birth cohorts. The common set of available and detectable exposure biomarkers and hormones analyzed in cord plasma are: 6 metals/trace elements, 3 polychlorinated biphenyl (PCB) congeners, hexachlorobenzene, dichlorodiphenyldichloroethylene and 2 perfluoroalkyl substances; and 3 thyroid, 3 reproductive and 2 metabolic hormones. Mixtures analyses were performed to assess each of the bilateral associations in the path exposures-hormones-birth weight, including mediation analysis. Combining all exposures, we found an inverse association between PCB 180 and birth weight. PCB 180 was positively associated with sex hormone-binding globulin (SHBG) and negatively associated with leptin and insulin. Similarly, thallium was positively associated with testosterone, estradiol, and SHBG, and negatively with insulin. Lead was positively associated with insulin. Higher free thyroxine (FT4), insulin, and leptin were associated with higher birth weight, whereas higher SHBG was associated with lower birth weight. Mediation analysis for PCB 180 indicated that 94% of the effect of this exposure on birth weight is mediated by FT4, SHBG, leptin, and insulin. Assessing the health risk of chemical mixture exposure reflects better real-world situations, thereby allowing more effective risk assessment. Our results suggest that hormonal markers are on the causal path in the association between environmental exposure and birth weight, adding interesting insights for mechanistic research. https://doi.org/10.1016/j.envint.2025.109700

The impact, mechanisms and prevention strategies of environmental endocrine disruptors on male reproductive health,
Han, X. Y. and Jin, X. L., *Frontiers in Endocrinology*, Oct 1 2025, Vol. 16.

Background Environmental endocrine disruptors (EEDs) including heavy metals, plasticizers, and persistent organic pollutants have been increasingly linked to declining male reproductive health globally. While epidemiological associations are well-established, the underlying molecular mechanisms and long-term consequences require systematic evaluation.Objectives This review synthesizes current evidence on EED impacts on male reproductive health, focusing on molecular mechanisms, population-based evidence, transgenerational effects, and intervention strategies.Methods We conducted comprehensive literature searches across PubMed, Web of

Science, and Scopus (2019-2024) to identify peer-reviewed studies on EED reproductive toxicity, including mechanistic investigations, epidemiological studies, and intervention research.Results EEDs disrupt male reproduction through multiple pathways: androgen and estrogen receptor interference, oxidative stress induction, mitochondrial dysfunction, and epigenetic modifications. Population studies demonstrate consistent associations between EED exposure and reduced sperm quality, with effect sizes varying by exposure level and chemical type. Animal studies provide compelling evidence for transgenerational inheritance of reproductive dysfunction through epigenetic mechanisms, though human evidence remains limited. Workplace protection measures, environmental remediation, and policy interventions show promise but require broader implementation. Conclusions EEDs pose significant threats to male reproductive health through complex, interconnected mechanisms. While substantial progress has been made in understanding these effects, critical gaps remain in mixture toxicology, low-dose effects, and transgenerational impacts in humans. Enhanced biomonitoring, mechanism-based interventions, and strengthened regulatory frameworks are essential for protecting current and future reproductive health. https://doi.org/10.3389/fendo.2025.1573526

Endocrine and Reproductive Health Considerations of Sunscreen UV Filters: Insights from a Comprehensive Review 2014-2024,
Jaskulak, M., Cinkusz, M., Franchuk, K. and Zorena, K., *Current Environmental Health Reports*, Aug 2 2025, Vol. 12, no. 1.

Purpose of Review Chemical (organic) ultraviolet (UV) filters-carbon-based compounds widely used in sunscreen formulations-are essential for protecting against harmful UV radiation. However, emerging evidence over the last decade (2014-2024) has raised concerns regarding their potential endocrine-disrupting effects, environmental persistence, and bioaccumulation. This comprehensive review evaluates the endocrine, reproductive, and developmental health impacts of organic UV filters, with a focus on benzophenone derivatives such as BP-3, BP-2, and 4-OHBP.Recent FindingsThe analysis incorporates data from 75 studies identified through PRISMA-guided screening of epidemiological and human research. Findings reveal significant hormonal disruptions, including reduced testosterone levels in adolescent males, altered thyroid hormones in pregnant women, and associations with delayed pubertal development in boys and early menarche in girls. Mixed exposures to multiple UV filters, frequently occurring in real-world scenarios, demonstrate cumulative and complex effects, particularly on thyroid hormone levels and reproductive health. In men, benzophenones are associated with decreased sperm quality and motility, while in women, their impact on ovarian reserve and fertility outcomes appears less pronounced. Prenatal exposure studies show mixed outcomes, ranging from reduced neonatal size and gestational age to increased placental-to-birth weight ratios. Summary This review underscores the dual nature of organic UV filters, emphasizing their importance in photoprotection while highlighting the need for a balanced approach to safety evaluations. Future research should prioritize long-term cohort studies, assessments of mixed exposure effects, and the development of safer alternatives. Addressing these challenges is crucial for mitigating risks to human health and the environment while maintaining the protective benefits of sunscreens. https://doi.org/10.1007/s40572-025-00492-9

Serum concentrations of perfluoroalkyl and polyfluoroalkyl substances and risk of ovarian cancer,
Jones, R. R., Madrigal, J. M., Medgyesi, D. N., Fisher, J. A., Calafat, A. M., Botelho, J. C., Kato, K., Albert, P. S., Silverman, D. T., Hofmann, J. N. and Trabert, B., *Jnci-Journal of the National Cancer Institute*, 2025.

Background Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are persistent, widespread environmental contaminants, and some are endocrine disrupting. Studies of gynecologic cancers are

limited; we evaluated ovarian cancer, a rare, often fatal malignancy.Methods This nested case-control study included 318 ovarian cancer cases and 472 individually matched female controls in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial, which recruited participants aged 55-74 years from 10 US study centers (1993-2001). We looked at cases through 2016 and quantitated 8 PFAS in prediagnostic serum samples. We estimated odds ratios (ORs) and 95% confidence intervals (CIs) for continuous (log2-transformed) and categorized PFAS concentrations by using conditional logistic regression models, implicitly adjusting for matching factors (age, center, year of random assignment, year of blood draw, race and ethnicity) and adjusting for smoking, body mass index, family history of cancer, menopausal hormone therapy and oral contraceptive use, parity, and number of freeze-thaw cycles.Results We found a positive association with ovarian cancer for a doubling in 2-(N-methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA) concentrations (OR for log2 = 1.24, 95% CI = 1.03 to 1.49) and 62% greater risk among those in the highest quartile (OR for quartile 4 vs quartile 1 = 1.62, 95% CI = 1.03 to 2.54; P for trend = .02). Perfluorooctane sulfonic acid (PFOS) was associated with increased risk (OR for log2 = 1.47, 95% CI = 1.05 to 2.06), with no quartile trend (P for trend = .79). Associations with perfluorononanoic acid (OR for log2 = 1.36, 95% CI = 0.95 to 1.95) and perfluorodecanoic acid (OR for log2 = 1.35, 95% CI = 0.94 to 1.95) were suggested, with nonmonotonic quartile trends (P for trend = .12 to .21). The MeFOSAA associations were strongest in women aged 55-59 years (OR for log 2 = 1.60, 95% CI = 1.13 to 2.27), more moderate in women aged 60-64 years (OR for log2 = 1.31, 95% CI = 0.90 to 1.90), and null among women 65 years of age and older (OR for log2 = 1.02, 95% CI = 0.73 to 1.43; P for heterogeneity = .22). Associations persisted in cases diagnosed 8 years or more after blood collection. Conclusions These findings offer novel evidence for PFAS as ovarian cancer risk factors, particularly PFOS and MeFOSAA, a PFOS precursor. https://doi.org/10.1093/jnci/djaf204

Evaluating health impacts of exposure to PFAS mixtures: a systematic review of epidemiological studies using mixture methods,
Kemp, M. J., Thoppe, K., Jones, K., Maltby, M., Ball, K. and Barlow, C. A., *Critical Reviews in Toxicology*, Sep 14 2025, Vol. 55, no. 8, p. 777-795.

Per- and polyfluoroalkyl substances (PFAS) continue to be an emerging chemical class of concern due to their long half-lives in nature and in the human body. There have been many epidemiology studies published in the scientific literature on PFAS and various health effects. Until recently, these studies have focused on assessing exposure to individual PFAS rather than exposure to mixtures of PFAS. Over the past two decades, mixture methods-statistical methods for investigating the association of mixtures-have been developed, making it possible to more accurately assess the risk of adverse health effects associated with exposure to PFAS. To help provide a resource for the overall evaluation of potential health effects of PFAS mixtures, we applied a consistent set of examination methods and criteria for all epidemiology studies that examined the potential relationship between exposure to PFAS mixtures and various types of health outcomes. We identified 233 cohort studies, 39 case-control studies, and 89 cross-sectional studies that evaluated general background-level exposures, exposure from contaminated sites, and occupational exposure to PFAS mixtures and health outcomes including metabolic, cardiovascular, and immune system effects, fetal development, pregnancy outcomes, reproductive effects, liver function, and respiratory effects. We extracted study characteristics and results in a systematic manner and performed a formal study quality evaluation and classified studies into tiers based on their methodological strengths and weaknesses. We found 42 prospective cohort studies, five nested case-control studies, and one traditional case-control study that qualified for inclusion in the highest tier of quality (Tier I). Overall, the weight of evidence from this systematic review indicates that the available epidemiology studies currently support an association between exposure to PFAS mixtures and

adiposity, increased total cholesterol, and hypertension, while the evidence for all other health outcomes is suggestive or limited. https://doi.org/10.1080/10408444.2025.2546427

Investigating the association between bisphenols and diabetes: Evidence from epidemiological and bioinformatics,
Li, J., Zhao, Y. P., Liu, H., Yang, P. P., Yang, S. and Liang, G. Y., *Ecotoxicology and Environmental Safety*, Oct 1 2025, Vol. 304.

Bisphenol A (BPA), widely employed in the manufacture of plastics, has been associated with the development of numerous diseases. Bisphenol F (BPF) and bisphenol S (BPS) have been introduced as common substitutes for BPA; however, their safety profiles remain contentious, particularly regarding potential associations with diabetes risk. This study aimed to evaluate the relationship between exposure to bisphenols (BPs) and the prevalence of diabetes among U.S. adults using data from the National Health and Nutrition Examination Survey (NHANES), and to investigate the molecular mechanisms underlying BPF-induced diabetes through integrated network toxicology, molecular docking, and mediation analysis. After adjusting for confounders including sex, age, race, and education level, a statistically significant association was observed between BPF exposure and diabetes prevalence (OR = 1.04, P = 0.032). Stratified analyses revealed age-dependent metabolic heterogeneity: BPF exposure exhibited a linear association with diabetes in individuals under 50 years (OR = 1.05, P = 0.042), while a non-linear association was observed in those aged 50 and above (P-overall = 0.000876; P-nonlinear = 0.031). Network toxicology and molecular docking analyses indicated that BPF may impair insulin resistance and lipid metabolism by interacting with key proteins (FN1, GAPDH, TP53) through stable hydrogen bonding and pi-pi stacking, with binding affinities ranging from-5.1 to-7.0 kcal/mol. Mediation analysis suggested a potential suppressive effect of triglycerides on the association between BPF and diabetes in older adults (>= 50 years), although the indirect effect was not statistically significant (IE = -0.008, 95 % CI: -0.019-0.003, P = 0.142). The negative mediation proportion (-12.1 %) indicated that the positive direct effect of BPF on diabetes (DE = 0.073, 95 % CI: 0.007-0.14, P = 0.031) was masked by triglycerides. These findings provide novel epidemiological and mechanistic insights into the link between BPF exposure and diabetes risk, underscoring the necessity for rigorous safety assessment of BPA substitutes in consumer plastics. https://doi.org/10.1016/j.ecoenv.2025.119105

Effects of single and multiple endocrine-disrupting chemical exposures on hyperactivity trajectories among preschoolers: A cohort study,
Li, R. Y., Li, S. Q., Zhou, Y., Xiao, W., Xu, H. Q., Tao, X. Y., Xie, J. A. and Wan, Y. H., *Environment International*, Oct 2025, Vol. 204.

Objective To evaluate the association of individual and mixed exposure to endocrine-disrupting chemicals (EDCs) with hyperactivity trajectories in preschoolers. Method This study used data from a cohort of 823 preschoolers. Baseline urine samples measured concentrations of 22 EDCs (T-0). Follow-ups occurred twice, every six months (T-1 and T-2), with mothers completing hyperactivity questionnaires at all time points (T-0-T-2). Latent class growth analysis (LCGA) was used to assess children's hyperactivity trajectories. We investigated the individual and joint effects of EDCs using binary logistic regression, quantile-based g-computation (Q-gcomp) model, and Bayesian kernel machine regression (BKMR) model, respectively. Results We identified two hyperactivity trajectories: the "high hyperactivity trajectory" and the "low hyperactivity trajectory". The binary logistic regression results showed that nine chemicals were significantly associated with hyperactivity trajectories (OR = 0.57 similar to 2.37, 95 % CI: 0.33-4.03). The Q-gcomp model showed a positive association between mixed EDC exposures and the hyperactivity trajectories (OR = 2.13, 95 % CI: 1.70-2.66). The BKMR model found a significant positive relationship between the EDC mixtures and

hyperactivity trajectories when all chemical concentrations were at or above their 55th percentile compared with the median. After stratification by gender, we found that exposure to EDC mixtures was more strongly associated with hyperactivity trajectories in girls. Conclusion The current study indicates the adverse health effects of exposure to mixtures of EDCs among preschoolers, and suggests gender specificity in these effects. This highlights the importance of focusing on multi-pollutant exposure in early childhood and taking targeted interventions.
https://doi.org/10.1016/j.envint.2025.109825

Personal care product use and risk of adult-onset asthma: Prospective cohort analyses of US Women from the Sister Study,
Lim, J., Chang, C. J., White, A. J., Lo, S., Wang, H. T., Goodney, G. A., Miao, R., Barochia, A., Sandler, D. P. and Wong, J. Y. Y., *Environment International*, Aug 2025, Vol. 202.

Background: Population studies have found associations between prenatal exposure to endocrine-disrupting chemicals (EDCs) in personal care products (PCPs) and childhood asthma; however, few have examined adultonset asthma. We investigated the associations between commonly used PCPs and the risk of adult-onset asthma in a prospective cohort study of U.S. women. Methods: We analyzed 39,408 participants from the Sister Study who self-reported their usage frequency of 41 PCPs in the 12-month period before baseline (2003-2009). In our combined PCP analyses, we used Least Absolute Shrinkage and Selection Operator (LASSO) to select key PCPs that predict the risk of adult-onset asthma. In group-specific analyses, PCPs were aggregated into four product groups (i.e., beauty, everyday hair, hygiene, and skincare products). Subsequently, we conducted latent class analysis to identify groups of participants with similar patterns of PCP use (e.g., infrequent (reference), moderate, and frequent). Multivariable Cox regression models were used to assess the associations between PCP use and incident adult-onset asthma. Results: Over an average 12.5-year follow-up, 1,774 incident asthma cases were identified. We found a positive association between combined PCP use and adult-onset asthma risk (moderate users, hazard ratio [HR] = 1.19 (95% confidence interval (CI):1.05,1.33) and frequent users, HR = 1.19 (95% CI:1.06,1.34)). In group-specific analyses, moderate (HR = 1.21 (95% CI:1.07,1.37)) and frequent (HR = 1.22 (95% CI:1.08,1.38)) users of beauty products had higher asthma risk compared to infrequent users. Similar associations were observed for hygiene (moderate: HR = 1.14 (95% CI:1.01,1.29) and frequent: HR = 1.20 (95% CI:1.06,1.36)) and skincare products (moderate: HR = 1.21 (95% CI:1.06,1.38) and frequent: HR = 1.20 (95% CI:1.06,1.35)). Conclusions: Our findings suggest that PCP use potentially contributes to future risk of adult-onset asthma among women.
https://doi.org/10.1016/j.envint.2025.109681

Associations between per- and polyfluoroalkyl substances (PFAS) exposure via infant feeding and the gut microbiota of preterm infants: A study of mother-preterm infant dyads,
Lin, B. C., Zhu, L., Xu, H., Xiao, Y. P., Xu, J. Q., Huang, Y. F., Yang, C. Z., Wang, M. Q., Bai, Z. J., Zhu, W., Wei, Y. H., Li, H. T. and Chen, Y. R., *Ecotoxicology and Environmental Safety*, Sep 15 2025, Vol. 303.

Infants are exposed to per- and polyfluoroalkyl substances (PFAS) via feeding, yet the influence of PFAS on their gut microbiota remains poorly understood. In this study, 73 mother-preterm infant dyads were recruited in Shenzhen. We measured concentrations of 13 PFAS (PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFBS, PFHxS, PFOS, HFPO-DA, ADONA, 6:2 Cl-PFESA, and 8:2 Cl-PFESA) in the feeding substances (breast milk or formula) at the fourth week postpartum. Concurrently, fecal samples from preterm infants were collected for analysis of gut microbiota and metabolites. The highest mean concentrations were observed for two short-chain PFAS: PFBA and PFPeA. Eleven out of the 13 PFAS had detection rates exceeding 50 % and were included in subsequent analyses. Linear

regression analysis indicated that daily intakes of PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFBS, and PFHxS were negatively associated with the ln-transformed PD_whole_tree index. Daily intakes of PFBA, PFBS, PFOA, and PFHxS were significantly linked with beta diversity. The genus Veillonella was more abundant in the upper tertile groups of PFBA and PFBS. Moreover, daily intakes of PFHpA and PFOA were linked to predicted microbiome functions. Pathway analysis further revealed that PFAS daily intake was associated with synthesis or metabolism of multiple nutrients (including vitamins and amino acids). Notably, linear regression demonstrated that PFAS daily intake was negatively associated with levels of docosapentaenoic acid and docosahexaenoic acid. Our findings suggest that PFAS exposure through feeding may adversely affect the gut microbiota and normal development of preterm infants, potentially posing health risks.
https://doi.org/10.1016/j.ecoenv.2025.118853

Prenatal microplastic exposure and umbilical cord blood androgenic and glucocorticoid hormones,
Liu, B. Y., Zheng, D. M., Wang, J., Wang, D., Zhang, S. and Chu, D. M., *Ecotoxicology and Environmental Safety*, Sep 15 2025, Vol. 303.

Placental microplastic exposure has emerged as a potential environmental risk factor affecting fetal development. This study investigates the association between placental microplastic burden and umbilical cord hormone levels in a cohort of pregnant women from Shenyang, China. A total of 1324 pregnant women during 2022-2023 were enrolled. Placental microplastics were quantified using a laser direct infrared (LD-IR) chemical imaging system, targeting polyvinyl chloride (PVC), polypropylene (PP), and polybutylene succinate (PBS). Umbilical cord blood cortisol, cortisone, dehydroepiandrosterone (DHEA), and androstenedione were analyzed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Regression models were applied to assess individual microplastic associations, while quantile-based g-computation (g-comp) and Bayesian Kernel Machine Regression (BKMR) were used to evaluate mixture effects. Microplastics were detected in all placental samples, with a median total concentration of 12 particles/10 g. Placental microplastic exposure was significantly associated with altered fetal hormone levels. Higher PVC, PBS, and total microplastic concentrations were linked to lower cortisol levels, while PVC, PP, and total microplastics were associated with reduced cortisone. In contrast, PBS and total microplastics were positively associated with DHEA, and PVC, PBS, and total microplastics correlated with increased androstenedione. The cortisol/DHEA and glucocorticoid/androgenic ratios were significantly reduced with higher microplastic exposure, suggesting endocrine disruption. Mixture analysis confirmed these trends, showing decreased glucocorticoids and increased androgens, with sex-stratified analysis indicating stronger cortisol reductions in boys and higher DHEA in girls. Overall, placental microplastic exposure was associated with altered fetal hormone levels, suggesting potential endocrine disruption while further studies are needed.
https://doi.org/10.1016/j.ecoenv.2025.118827

Multielemental Profile for Seminal Plasma Through Inductively Coupled Plasma-Tandem Mass Spectrometry and Its Relationship with Seminal Parameters, Spermatic Biomarkers, and Oxidative Stress,
López-Botella, A., Cenitagoya-Alonso, N., Sánchez-Romero, R., Sáez-Espinosa, P., Hernández-Falcó, M., Gómez-Torres, M. J. and Todoli-Torró, J. L., *Antioxidants*, Sep 15 2025, Vol. 14, no. 9.

The present study investigated the decline in human fertility by analyzing the multielemental profile of seminal plasma and its relationship with seminal parameters and sperm biomarkers. Twenty-nine donor seminal plasma samples were examined using inductively coupled plasma-tandem mass spectrometry (ICP-MS/MS). Method optimization demonstrated that robust plasma conditions,

including internal standardization and helium (He) collision gas, were essential to achieve reliable quantification. These conditions mitigated matrix effects and spectroscopic interferences, despite lower sensitivity. Elements such as copper (Cu), iron (Fe), manganese (Mn), strontium (Sr), titanium (Ti), vanadium (V), and chromium (Cr) were quantified, and several significant correlations were identified. Specifically, Cu was negatively correlated with seminal volume and positively correlated with sperm concentration and spontaneous acrosome reacted sperm, but negatively correlated with medium mitochondrial membrane potential (MMP); Mn showed negative associations with sperm vitality and medium MMP; Fe showed a negative correlation with motile sperm concentration (4 h); V was positively correlated with acrosome reacted sperm after acrosome reaction induction and with very low/medium MMP, whereas it was negatively associated with tyrosine phosphorylation; and Cr also showed a negative correlation with tyrosine phosphorylation. As, Mo, and Pb were detected in a few samples, limiting correlation analysis. From a functional perspective, elements such as As and Pb, as well as excess Cu or Fe, may contribute to oxidative stress by enhancing reactive oxygen species (ROS) generation and impairing antioxidant defenses. Conversely, essential metals, including Mn and Cu, at physiological concentrations act as cofactors of antioxidant enzymes and play a protective role against oxidative damage.
https://doi.org/10.3390/antiox14091118

Randomised controlled trial of a low plastic diet and lifestyle intervention for adults with cardiometabolic risk factors: the Plastic Exposure Reduction Transforms Health (PERTH) trial - a protocol,
Lucas, A., Harray, A., Duong, L., Herrmann, S., Vlaskovsky, P., Trevenen, M., Chan, D., Papendorf, H., Smith, T., Flint, L., Liu, A., Gaudieri, S., Wang, X. Y., Mueller, J. F., Thomas, K., Murray, K., Symeonides, C., Dunlop, S., Watts, G. and Lucas, M., *Bmj Open*, Aug 25 2025, Vol. 15, no. 8.

Introduction Phthalates and bisphenols, chemicals commonly used in the production of plastic products, exhibit endocrine disrupting properties linked to obesity and systemic inflammation. Given the ubiquitous use of plastic chemicals, their adverse impact on human health is of great importance. In this protocol, we describe a randomised controlled trial aimed at testing whether minimising exposure to plastics and plastic-associated chemicals (PACs) in community-dwelling adults with cardiometabolic risk factors can reduce urinary excretion of PACs and improve cardiometabolic health. Methods and analysis The study will recruit (n=60) community-dwelling adults (18-60 years) with cardiometabolic risk factors, characterised by a body mass index of >= 30 kg/m(2) and waist circumference of >= 88 cm in women and >= 102 cm in men. Participants will be randomised to a control (n=30) or an intervention group (n=30) receiving a 4-week diet and lifestyle modification designed to reduce plastic exposure, which includes the replacement of all food, kitchen utensils and equipment, personal care and cleaning products. The primary outcome is a reduction in urinary excretion of bisphenols after the 4-week intervention compared with the control arm. The secondary outcomes are the reduction in urinary excretion of low and high molecular weight phthalates. Finally, tertiary outcomes investigate improvements to cardiometabolic biomarkers, body composition, waist circumference and blood pressure. Participants will self-collect urine, stool and nasal lavage samples a day before beginning the intervention and at the end of each week. Fasting blood samples and health assessments will be collected during clinic visits: at baseline, mid-point and a day after the intervention period. Urinary PAC excretion and cardiometabolic health outcomes will be compared between the intervention and control groups. Ethics and dissemination The PERTH Trial has ethics approval from the University of Western Australia Human Research Ethics Committee; 2021-ET001118. Results will be submitted for publication in peer-reviewed journals and presented at conferences. Trial registration number NCT06571994. https://doi.org/10.1136/bmjopen-2025-099330

Endocrine-disrupting chemicals exposure: cardiometabolic health risk in humans,
Ma, C. X., Ma, X. N., Li, H. L., Mauricio, D. and Fu, S. B., *Cardiovascular Diabetology*, Oct 1 2025, Vol. 24, no. 1.

Endocrine-disrupting chemicals (EDCs) are exogenous compounds that interfere with hormone action, and growing evidence suggests that human exposure to certain EDCs may increase the risk of obesity, type 2 diabetes mellitus (T2DM), and cardiovascular disease (CVD). To clarify the impact of EDC exposure on cardiometabolic health, we conducted a review of the literature (2005-2025) to identify both human epidemiological studies and animal mechanistic studies. In this narrative review, we primarily summarize the existing human epidemiological evidence on the cardiometabolic effects of EDCs, while also considering mechanistic insights, including selected animal studies, to illustrate biological plausibility. Key findings indicate that EDC exposures are consistently associated with elevated risks of cardiometabolic conditions. Notably, prenatal and early-life EDC exposures appear to increase susceptibility to obesity, impaired glucose metabolism, and cardiovascular dysfunction later in life, while adult exposures are linked to a higher incidence of metabolic syndrome, type 2 diabetes, and related cardiovascular complications. In conclusion, this review underscores EDC exposure as a significant environmental risk factor for cardiometabolic disease. Accordingly, strengthening regulatory policies to reduce human exposure to these chemicals-alongside further research into underlying mechanisms-may be crucial for improving cardiometabolic health outcomes. https://doi.org/10.1186/s12933-025-02938-8

Molecular Alterations in Semen of Per-And Polyfluoroalkyl Substance Exposed Subjects: Association Between DNA Integrity, Antioxidant Capacity and Lipoperoxides,
Marinaro, C., Bianchi, A. R., Guerretti, V., Barricelli, G., Berman, B., Bertola, F., Micali, S., Busardò, F. P., Di Giorgi, A., De Maio, A., Piscopo, M., Montano, L. and Lettieri, G., *Antioxidants*, Jun 27 2025, Vol. 14, no. 7.

In the last decades, there has been huge interest in Per- and Polyfluoroalkyl Substances (PFAS) worldwide because of the toxic effects on humans. In 2013, a large-scale contamination of PFASs in the Veneto region was caused by a fluorochemical plant in Vicenza. About 130,000 inhabitants were exposed to PFAS in their drinking water. To date, relatively few studies have investigated the associations between blood serum PFAS concentrations and oxidative stress in semen. This study compared the antioxidant activity, lipoperoxide levels and protection or induction of oxidative DNA damage by sperm nuclear basic proteins (SNBP) in subjects living in Veneto exposed to PFAS (VNT) with those living in a non-PFAS contaminated area (VSL). Although the semen parameters were within the WHO range, the VNT semen samples showed higher levels of lipoperoxides and lower antioxidant activity compared to the VSL samples. These differences were statistically significant. We also examined DNA damage following SNBP addition under pro-oxidative conditions, finding a significantly different distribution of DNA damage types between the two groups, where 0 means no damage and 1 to 3 means increasing damage with 3 indicating maximum damage. SNBP of VNT subjects showed a reduced ability to protect DNA from oxidative damage. In the VSL group, damage 0 was found in 56% of subjects, 35% of the VNT group show damage 1, 36% damage 2 and 18% damage 3, while only 11% of VNT subjects show damage 0. Additionally, VNT with 0-grade DNA oxidative damage also exhibited reduced antioxidant activity and higher levels of lipoperoxides, in contrast to VSL. The results of this study indicate that exposure to PFAS produces oxidative stress in the semen of VNT subjects, who were also found to have blood serum perfluorooctanoic acid (PFOA) levels above the threshold. This suggests the possibility of infertility issues and emphasises the necessity for additional research into the long-term consequences of oxidative stress on male fertility and the health of offspring. https://doi.org/10.3390/antiox14070792

Endocrine disruptive chemicals (EDCs) and autoimmune thyroid diseases (AITD): A systematic literature review,
Monaghan, M., Rodrigues, S., Sharma, S., Leung, A. M. and Van Gerwen, M., *Current Opinion in Endocrine and Metabolic Research*, Dec 2025, Vol. 41.

The association between endocrine disruptive chemicals (EDCs) and autoimmune thyroid disease (AITD) has not been well established. This systematic review aimed to summarize existing literature and provide an up-to-date overview of EDCs and their association with AITD. A search of the National Library of Medicine PubMed and Scopus databases was completed to identify relevant articles published in English through September 2024. A total of 4 studies met inclusion criteria. Results of the included studies varied, ranging from significant positive to significant negative associations with AITD for different EDCs. This comprehensive review highlights the limited knowledge of this association. Besides investigating individual EDCs, it is important to include dose - response studies and exposures to EDC mixtures. https://doi.org/10.1016/j.coemr.2025.100585

Endocrine disrupting chemicals in maternal and umbilical cord plasma and their associations with birthweight in the GUSTO cohort,
Ng, S., Chen, L. W., Chen, Z. Y., Chen, M. H., Chu, A. H. Y., Godfrey, K. M., Tan, K. H., Gluckman, P. D., Eriksson, J. G., Yap, F., Chen, P. C., Chong, Y. S., Chen, C. Y. and Chan, S. Y., *Environmental Health*, Aug 18 2025, Vol. 24, no. 1.

Background With daily exposure to multiple endocrine disrupting chemicals (EDCs), understanding individualized co-exposure patterns could better identify chemicals that threaten health. This is particularly pertinent for the vulnerable fetus during in-utero development, where exposure can have long lasting health consequences. As there is limited information of EDC exposure in Asian maternal-offspring populations, this study aimed to (1) determine levels of a selected range of EDCs (focusing on Substances of Very High Concern by the European Chemical Agency) in maternal and corresponding cord blood plasma, (2) investigate the sociodemographic factors associated with plasma EDC concentrations, and (3) associate EDC-mixtures with birthweight, in a Singapore cohort. Methods Targeted liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used to determine the concentration of 30 chemicals of interest in 780 maternal and 782 cord plasma samples collected at delivery in the multi-ethnic Asian (Chinese, Malay, Indian) mother-offspring GUSTO study. Quantile-based g-computation was used to estimate the combined effect of chemical mixtures and its association with birthweight. Results Twenty-seven out of the thirty selected chemicals were reliably detected in both maternal and cord plasma. Perfluorooctanesulfonic, perfluorooctanoic, perfluorobutanesulfonic and perfluorobutanoic acids (PFOS, PFOA, PFBS, PFBA, respectively) were the predominant perfluoroalkyl acids (detected in > 90% of samples), while mono (2-ethylhexyl) phthalate (MEHP) and monobutyl phthalate were the main phthalate metabolites (detected in > 99% of samples). Concentrations of fourteen chemicals, including PFBA, PFBS and bisphenol S (BPS) were higher in cord plasma than in corresponding maternal plasma; eight being > 1.5 times higher (ranging from 1.75 to 2.93). A mixture of chemicals in cord plasma associated with higher birthweight [116.5 g (95%CI 3.1, 229.9) per quantile increase], but no association was observed for the maternal mixture. Further, different chemicals from the same EDC group in either cord or maternal plasma showed associations in opposite directions with birthweight. Discussion Our results suggest substantial transplacental transfer and fetal accumulation of many chemicals, particularly the newer replacement compounds. Stronger associations with birthweight were found for the cord chemical mixture than for the maternal mixture, supporting the idea that these chemicals may have direct effects in the fetus to influence growth. Moreover, individual chemicals within each EDC group appear to have different mechanisms of effect resulting in divergent associations with birthweight. Conclusion This study adds to the growing concern about the impact

of EDCs, especially the newer chemicals on vulnerable groups such as the developing fetus, warranting further research on the potential effects of in-utero EDC exposure on child health.
https://doi.org/10.1186/s12940-025-01202-6

Serum levels of per- and polyfluoroalkylated substances and methylation of DNA from peripheral blood,
Omichessan, H., Dragic, D., Perduca, V., Truong, T., Polidoro, S., Kvaskoff, M., Cano-Sancho, G., Antignac, J. P., Baglietto, L., Mancini, F. R. and Severi, G., *Frontiers in Public Health*, Jul 28 2025, Vol. 13.

<bold>Background:</bold> Perfluorooctanoic acid (PFOA) and Perfluorooctane sulfonate (PFOS) are among numerous chemicals in the Per- and polyfluoroalkylated substances (PFAS) group, which are commonly present in various consumer and industrial products. These chemicals are recognized for their persistency, the ability to accumulate in biological systems and their documented adverse effects on human health. Previous research, which has primarily centered on global methylation patterns, has suggested that some effects of PFAS on human health may be linked to modifications in DNA methylation (DNAm). The aim of our study was to assess the relationship between the serum levels of PFOS and PFOA and CpG site-specific methylation of DNA from peripheral blood. <bold>Methods:</bold> We used a case-control study on breast cancer nested within the E3N cohort, a prospective study of French women, in which we measured DNAm at more than 850,000 CpG sites with the Illumina Infinium MethylationEPIC BeadChip for 166 case-control pairs. Serum levels of PFOS and PFOA were measured by liquid chromatography coupled to tandem mass spectrometry. <bold>Results:</bold> We found 64 CpG sites with significant hypomethylation or hypermethylation associated with increased levels of PFOA or PFOS (p-value(Bonferroni) < 0.05). The strongest association was found between PFOA serum levels and decreased DNAm at cg06874740 (p-value(Bonferroni) = 2.2x10(-5)) and between PFOS serum levels and decreased DNAm at cg02793158 (p-value(Bonferroni) = 9.3x10(-5)). Gene-set enrichment analyses using all CpG sites associated with PFOA or PFOS with an unadjusted p-value <0.01, identified 20 KEGG pathways for each of these compounds. <bold>Conclusion:</bold> PFAS exposure may be linked to substantial and widespread changes in the methylome that may be involved in the consequences on health of these pollutants. Our findings indicate that the biological and health effects of PFOA and PFOS may be more intricate and varied than previously thought, reinforcing the need for policies aimed at regulating this class of endocrine-disrupting chemicals.
https://doi.org/10.3389/fpubh.2025.1621495

Impact of plastic-related chemicals on emotional and behavioral health in children from Poland,
Polanska, K., Jankowska, A., Bury, D., Moos, R. K., Pälmke, C., Jerzynska, J., Jurewicz, J., Bose-O'reilly, S., Koch, H. M. and Garí, M., *Environmental Health*, Oct 14 2025, Vol. 24, no. 1.

BackgroundExposure to phthalates and non-phthalate plasticizers as well as bisphenols may be relevant to the development of behavioural symptoms in childhood with sex-specific effects, although the results of existing studies are not consistent. The aim of the study was to evaluate the cross-sectional association between childhood exposure to these compounds and behavioral outcomes in the REPRO_PL cohort (Poland).MethodsBehavioral assessments were performed at the age of 7-9 years by parents using the Strengths and Difficulties Questionnaire (SDQ). HPLC-MS/MS was used for the quantification of BPA and 21 phthalate metabolites corresponding to 11 phthalate compounds (n = 400) and their replacement alternatives BPF, BPS, three metabolites of diethylhexyl terephthalate (DEHTP) and three metabolites of di-isononyl-cyclohexane-1,2-dicarboxylate (DINCH) (n = 150). Multivariable linear regression models accounting for sex-specific effects as well as sex-adjusted models were applied, using both separate models for each metabolite (or sum of

metabolites) and joint models. In addition, mixtures models adjusted by the three chemical groups studied were also performed.ResultsMedian concentrations of several phthalate metabolites and bisphenols were of 42 mu g/L (MEP), 4.5 mu g/L (MMP), 3.5 mu g/L (Sigma DiDP), 2 mu g/L (BPA) and 1 mu g/L (BPF). For Sigma DEHTP and Sigma DINCH, the median concentrations were 35 mu g/L and 3.1 mu g/L, respectively. Exposure to phthalates was related to behavioral problems in girls, and bisphenols and DEHTP in boys. Among girls, DiBP was associated with mental health problems (total difficulties: beta = 4.84; 95% CI 0.72;8.96, emotional: beta = 2.14; 95% CI 0.33;4.0, hyperactivity/inattention: beta = 2.52; 95% CI 0.55;4.49, externalizing behavior: (beta = 2.95; 95% CI 0.36;5.53) and DiDP with hyperactivity/inattention scores (beta = 2.46; 95% CI 0.30;4.63). BPF was associated with emotional problems and internalizing behavior among boys in both main and sensitivity models (main model: beta = 1.03; 95% CI -0.16;2.21 and beta = 1.71; 95% CI -0.14;3.56 respectively).ConclusionsThis study shows that children's exposure to several replacement compounds of BPA and phthalates, such as BPF and DEHTP, are associated with adverse effects on school-age children's behavior, with a divergent sex-specific effect. In any case, mixture models did not provide any further insight on the aforementioned cross-sectional associations and further methodological approaches are needed to explore adverse neurodevelopmental outcomes in children and teenagers. https://doi.org/10.1186/s12940-025-01210-6

Paraben exposures and satiety hormones in preschool children: an ENVIRONAGE study,
Reimann, B., De Ruyter, T., Sleurs, H., Rasking, L., Verheyen, L., Giesberts, N., Pirard, C., Charlier, C., Frost, G., Vineis, P., De Henauw, S., Michels, N., Nawrot, T. S. and Plusquin, M., *Environmental Research*, Nov 15 2025, Vol. 285.

Background: Exposure to environmental pollutants has been associated with obesogenic effects, yet evidence in young children remains sparse. Parabens, widely used as antimicrobial preservatives in personal care products, may disrupt satiety hormones during early life, potentially influencing long-term metabolism and weight regulation. Methods: This cross-sectional study analyzed urinary methyl, ethyl, propyl, and butylparaben (MeP, EtP, PrP, BuP) levels in 4-6-year-old children from the ENVIRONAGE birth cohort using ultra-performance liquid chromatography/tandem mass spectrometry. Plasma satiety hormones (leptin, pancreatic polypeptide, glucagon-like peptide 1, and peptide YY) were measured via (radio-)immunoassays. Associations were assessed in 188 samples using covariate-adjusted linear regression, sex-stratified analysis, and mixture modeling (quantile g-computation and Bayesian kernel machine regression). Additionally, the role of BMI was investigated by partial correlation analysis. Results: As more than 96 % of the BuP measurements were below the LOQ, only the values of MeP, EtP and PrP were used for further statistical analysis. A doubling in PrP was associated with an 5.34 % [95 % Confidence Interval: 1.58 %, 9.23 %] increase in leptin, and BKMR indicated a positive linear association between parabens and leptin. Additional sensitivity analyses were indicative of sex-specific differences in the relationship between parabens, BMI and leptin levels. Conclusions: PrP may increase leptin levels, contributing to obesogenic effects in young children. Given rising childhood metabolic disorders, further longitudinal studies are needed to assess PrP exposure risks in personal care products.
https://doi.org/10.1016/j.envres.2025.122300

Associations between chronic exposure to bisphenols and parabens and gut microbiota in children,
Rodrigo, L., Bressa, C., Larrosa, M., Ramírez, V., Gil-Izquierdo, A., Sánchez-Muñoz, C., Martínez-Burgos, M. A., Zafra-Gómez, A. and Rivas, A., *Environmental Research*, Nov 15 2025, Vol. 285.

Bisphenols and parabens are endocrine-disrupting chemicals widely used in food packaging and personal care products. Early-life exposure to these compounds has been associated with adverse

health effects, but their potential role in modulating the gut microbiota during childhood remains poorly understood. The objective of this study was to investigate the association between chronic exposure to bisphenols and parabens and gut microbiota diversity, composition, and function in children. A cross-sectional study in 97 Spanish children aged 4-12 year was conducted. Bisphenols and parabens in hair were quantified using ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). Gut microbiota composition was assessed via 16S rRNA gene sequencing, and functional potential was inferred using PICRUSt2. Associations were explored using linear regression and random forest models, adjusting for age and sex. Total bisphenols and parabens were detected in 100 % of the children, with median concentrations of 311.33 ng/g and 1904.11 ng/g, respectively. No significant differences in overall gut microbiota diversity were observed between children with low and high exposure levels to bisphenols and parabens. However, regression models revealed associations between specific microbial genera and individual compounds. Additionally, bisphenol S was negatively associated with a predicted microbial pathway involved in methionine metabolism. Notably, Lachnospiraceae_UCG-001 emerged as a predictive genus for propylparaben exposure. Although gut microbiota composition was similar across exposure levels, specific taxa and functional pathways were linked to chronic bisphenol and paraben exposure. These findings support the need for further research on the health implications of early-life exposure to these endocrine-disrupting chemicals.
https://doi.org/10.1016/j.envres.2025.122643

Beyond Genes: Mechanistic and Epidemiological Insights into Paternal Environmental Influence on Offspring Health,
Rotem, R. S., Hernández-Díaz, S., Hauser, R. and Weisskopf, M. G., *Current Environmental Health Reports*, Aug 9 2025, Vol. 12, no. 1.

Purpose of ReviewIt is widely accepted that maternal genes and the in-utero environment can impact offspring's health. While fathers have long been considered mere conduits of genetic information, emerging evidence suggests that the paternal preconception environment can also affect offspring's health. This review delves into the biological mechanisms, beyond DNA inheritance, by which paternal preconception exogenous exposures can shape offspring outcomes, and factors that influence these mechanisms. We also discuss practical and methodological hurdles in epidemiological studies of male lineage inheritance.Recent FindingsA wide range of paternal exposures, from environmental pollutants to diet and lifestyle factors, have been linked with offspring's health. Several biological mechanisms, including epigenetic modifications in sperm, alterations in seminal fluid microbiome, and changes in the chemical composition of semen, may mediate these effects. Currently, most data come from animal models. Human research is hindered by difficulties in establishing and maintaining cohorts, accurately assessing paternal exposures, untangling the complex interactions among epigenetic mechanisms, and defining relevant exposure windows.SummaryFathers play a more significant role in shaping their children's health than previously thought. By unraveling the complex mechanisms underlying paternal environmental and genetic influence, we can potentially unlock new opportunities for transgenerational disease prevention and health promotion. The knowledge gained can empower the design of precision environmental health interventions that benefit future generations.
https://doi.org/10.1007/s40572-025-00488-5

Associations between urinary biomarkers of phthalates and phthalate alternatives and female sexual function in a North American cohort,
Schildroth, S., Bond, J., Wesselink, A. K., Koenig, M. R., Calafat, A. M., Botelho, J. C., Abrams, J. and Wise, L. A., *Journal of Sexual Medicine*, Oct 2025, Vol. 22, no. 10, p. 1766-1779.

Background Phthalates are endocrine-disrupting chemicals that can dysregulate hormonal systems supporting female sexual function (eg, estrogen interference). Female sexual function is important for positive sexual expression, fertility, and well-being but remains understudied in the context of environmental toxicants to which females are ubiquitously exposed. Identifying environmental determinants of female sexual dysfunction can inform exposure-reduction strategies and clinical practice to improve sexual health.Aim We investigated associations between phthalate exposure and sexual function in a cohort of North American females.Methods We leveraged cross-sectional data from a subset of 21-45-year-old females trying to conceive enrolled in Pregnancy Study Online (n = 347) to assess associations between phthalate and phthalate alternative exposure and sexual function, measured on a modified version of the Female Sexual Function Index-6 (FSFI-6). We summed FSFI-6 responses (range = 2-30); lower scores reflected poorer function. We measured urinary concentrations of 18 phthalate and alternative metabolites using online solid phase extraction coupled with high-performance liquid chromatography isotope dilution tandem mass spectrometry. Given that the biomarkers were nonlinearly associated with FSFI-6 scores, we categorized creatinine-corrected biomarker concentrations in tertiles. We used multivariable linear regression to estimate mean differences (beta) with 95% confidence intervals (CIs) in FSFI-6 scores per tertile increase in biomarker concentrations, adjusting for hypothesized confounders. In secondary analyses, we considered individual FSFI-6 items (range = 1-5) as outcome variables.Outcomes Female sexual function measured on the FSFI-6.Results Most biomarkers were not associated with FSFI-6 scores. Mono-n-butyl phthalate concentrations were weakly and non-monotonically associated with lower summed FSFI-6 scores (beta = -0.8, 95% CI = -1.8, 0.2) and orgasm scores (beta = -0.3, 95% CI = -0.7, 0.1) at the second (vs first) tertile, reflecting poorer sexual function. Mono-2-ethyl-5-carboxypentyl terephthalate concentrations were weakly associated with poorer scores for orgasm, while other biomarkers (notably, mono-carboxyisononyl phthalate) were associated with higher summed FSFI-6 and FSFI-6 item scores.Clinical Implications Exposure to phthalates should be considered in clinical settings, particularly for females experiencing issues with sexual function.Strengths and Limitations This study represents one of the first to assess associations of phthalate exposure and female sexual function, and we investigated associations in an established cohort with a validated measure of sexual function. We were limited by our sample size and cross-sectional study design.Conclusion Although associations for most phthalate biomarkers were null, some were weakly associated with female sexual function, suggesting exposure to certain chemicals may affect female sexual function with implications for clinical practice and exposure reduction strategies. https://doi.org/10.1093/jsxmed/qdaf205

Chemical disruption of placental thyroid hormone signalling: a systematic review that highlights sex-specific effects,
Swan, J., Zhurenko, D., Huttunen, K. M. and Rysä, J., *Archives of Toxicology*, 2025.

Thyroid hormones are crucial for growth, brain development, metabolism, and organ maturation in developing foetuses. Until 12-14 weeks of gestation, the foetus depends on maternal thyroid hormones before its own thyroid gland begins functioning. Environmental chemical and medication exposure during pregnancy may affect the thyroid hormone supply to the foetus by interfering with placental transport carriers and metabolism. This systematic review evaluated chemical effects on thyroid hormone passage from maternal to foetal circulation, modulated by transporters and enzymes. A search of PubMed, Scopus, and Web of Science identified 24 relevant studies published between 1900 and 2024, including 4 epidemiological studies, 8 in vivo animal studies, and 15 in vitro studies. The review found evidence that persistent organic pollutants, flame retardants, endocrine disrupting chemicals, pharmaceuticals, and other substances can disrupt placental thyroid hormone signalling through various mechanisms. These include alterations in transporter expression and enzyme activity in the placenta. Several studies observed sex-specific effects, with male and female

foetuses showing different responses to chemical exposure. In some cases, sex differences were in the degree of change, while in others, the same chemical had opposite effects based on foetal sex. However, many studies used choriocarcinoma cell lines, which may not fully replicate human placental processes. This review highlights the need for further research to elucidate chemical exposure's impact on foetal thyroid hormone status and the role of foetal sex using human physiologically relevant models. https://doi.org/10.1007/s00204-025-04203-z

Association between exposure to perfluoroalkyl compounds during early pregnancy and risk of late miscarriage: The Japan Environment and Children's Study,
Tatsuta, N., Iwai-Shimada, M., Isobe, T., Nakayama, S. F., Sekiyama, M., Takagi, M., Kobayashi, Y., Taniguchi, Y., Yamazaki, S. and Japan Environm Childrens Study, G., *International Journal of Hygiene and Environmental Health*, Sep 2025, Vol. 270.

Objective: Previous studies have suggested that perfluoroalkyl and polyfluoroalkyl substances (PFAS) could be related to the occurrence of miscarriages, but the results are inconclusive. Therefore, this study aimed to assess the effects of PFAS exposure during the first trimester on miscarriages that occurred between 12 and 22 weeks of gestation. Methods: The participants were mothers and infants that registered for the Japan Environment and Children's Study. Twenty-eight PFAS, including perfluorooctanoic acid, perfluorohexane sulfonate, and perfluorooctane sulfonate, were identified in the plasma collected from pregnant participants. Miscarriage information was transcribed from the medical records. A propensity score was used to select the control group (mothers that gave live births), that matched the miscarriage group. The detection and concentrations of the PFAS in the miscarriage and control groups were compared. Results: Among 24,412 pairs of maternal PFAS measurements, 66 miscarriages (0.3 %) were documented. No significant differences in the detections or concentrations of PFAS were found between the miscarriage and live birth groups ($p > 0.196$). Conclusions: No association between prenatal PFAS exposure and late miscarriage was observed. Further studies are required owing to the small sample size. https://doi.org/10.1016/j.ijheh.2025.114673

Associations Between Endocrine-Disrupting Chemical Exposure and Fertility Outcomes: A Decade of Human Epidemiological Evidence,
Tzouma, Z., Dourou, P., Diamanti, A., Harizopoulou, V., Papalexis, P., Karampas, G., Liepinaitiene, A., Dedele, A. and Sarantaki, A., *Life-Basel*, Jun 21 2025, Vol. 15, no. 7.

Endocrine-disrupting chemicals (EDCs) are exogenous compounds that interfere with the endocrine system by mimicking or blocking the action of endogenous hormones such as estrogens, androgens, and thyroid hormones. This systematic review aims to evaluate the current epidemiological evidence linking EDC exposure with adverse reproductive outcomes in males and females of reproductive age. A total of 14 observational studies published between 2014 and 2024 were included following structured searches in PubMed, Scopus, and Google Scholar. The most commonly studied EDCs included bisphenol A (BPA), its analogs (such as bisphenol S, BPS), phthalates, parabens, per- and polyfluoroalkyl substances (PFAS), and persistent organic pollutants (POPs). The review found consistent associations between EDC exposure and multiple reproductive endpoints, such as impaired semen quality, decreased ovarian reserve, infertility, polycystic ovary syndrome (PCOS), altered hormone levels-specifically estradiol (E2), luteinizing hormone (LH), and follicle-stimulating hormone (FSH)-and adverse outcomes in assisted reproductive technologies (ART), including in vitro fertilization (IVF). Despite methodological heterogeneity, the findings support the biological plausibility of EDCs in disrupting reproductive function. The review highlights the urgent need for regulatory measures, increased public awareness, and longitudinal studies to assess the cumulative effects of chronic EDC exposure on human fertility. https://doi.org/10.3390/life15070993

Birth weight in relation to maternal and neonatal biomarker concentration of perfluorooctane sulfonic acid: a meta-analysis and meta-regression from a systematic review,
Wright, J. M., Rappazzo, K. M., Ru, H., Lee, A. L., Dzierlenga, M. W., Bateson, T. F. and Radke, E. G., *Journal of Exposure Science and Environmental Epidemiology*, 2025.

BackgroundPerfluorooctane sulfonic acid (PFOS) is a legacy chemical, that while banned in some countries, is still found in various environmental media and in nearly all humans given its long half-life.ObjectiveWe examined mean birth weight (BW) differences in relation to PFOS exposure biomarkers using systematic review methods.MethodsWe fit a random effects model to obtain the overall pooled effect and for stratified analyses examining biomarker sample type and timing, study confidence, scaling factors, and country of study origin. We also conducted a meta-regression to assess the impact of gestational age and other factors on the overall pooled effect.ResultsWe found a 30-gram BW deficit (beta = -30.3 g; 95%CI: -41.6, -18.9) with each ln-unit PFOS increase based on 53 studies identified in the systematic literature review. We detected BW deficits across all study confidence levels (beta range: -27 to -37 g per ln-unit increase) with the largest deficit in the medium confidence grouping (beta = -36.6 g; 95%CI: -56.3, -16.8). We did not see evidence of a gradient of BW deficits across biomarker sample timing (beta range: -24 to -39 g per ln-unit increase), but the smallest deficit in our primary analyses was detected for the 18 early sample timing studies (beta = -23.6 g; 95%CI: -38.7, -8.6). Robust deficits were also seen across various subgroups including by geographical region of study origin (e.g., Asian studies), more restrictive early biomarker sample collection, and post-partum samples (beta range: -16.9 to -30.6 g). For meta-regression analyses, none of the investigated factors explained significant heterogeneity across studies.ImpactWe detected a statistically significant BW deficit of 30 grams per each ln-unit PFOS increase across all 53 studies in our meta-analysis; results were comparable in magnitude across study confidence, sample timing, and other strata. Unlike previous meta-analyses based on fewer studies, our results suggest that pregnancy hemodynamics do not fully explain the overall association. Characterization of the potential risk of developmental effects related to PFOS and other legacy chemicals will have important risk assessment and risk management ramifications in the future. https://doi.org/10.1038/s41370-025-00798-8

Prenatal exposure to polycyclic aromatic hydrocarbons and the risk of childhood overweight,
Yang, Y., Liu, M. H., Shao, H., Jiang, H. F., Yang, L. and Zhang, X. X., *Ecotoxicology and Environmental Safety*, Sep 15 2025, Vol. 303.

Polycyclic aromatic hydrocarbons (PAHs) are widespread environmental pollutants with endocrine-disrupting properties. Prenatal exposure to PAHs has been linked to metabolic alterations, but its long-term impact on childhood overweight risk remains unclear. This is the first large-scale study to comprehensively assess the impact of prenatal exposure to urinary polycyclic aromatic hydrocarbons (PAHs) on early childhood overweight and obesity outcomes using advanced mixture modeling approaches. Conducted in Shenyang, China, we enrolled 5600 mother-child pairs with maternal urine samples collected in the third trimester to quantify 11 PAH metabolites using HPLC-MS/MS. Children's weight and height were measured between the ages of 4 and 6 years to calculate BMI and determine overweight status based on the Chinese National Standards. Multivariable linear regression analyses revealed significant positive associations between several individual urinary OH-PAH metabolites and increased weight in children after adjusting for confounders. Notably, 2-hydroxynaphthalene (beta = 0.139, 95 % CI: 0.078, 0.201), 3-hydroxyfluorene (beta = 1.709, 95 % CI: 0.932, 2.486), 9-hydroxyphenanthrene (beta = 3.733, 95 % CI: 1.885, 5.581), 1-hydroxypyrene (beta = 0.914, 95 % CI: 0.003, 1.825), and 9-hydroxybenzo[a]pyrene (beta = 2.102, 95 % CI: 0.270, 3.934) were significantly linked with higher weight. Total OH-PAHs also showed a robust association (beta

= 0.110, 95 % CI: 0.066, 0.154). Similar positive associations were observed for BMI, including 2-hydroxynaphthalene (beta = 0.090, 95 % CI: 0.027, 0.153), 3-hydroxyfluorene (beta = 1.464, 95 % CI: 0.665, 2.263), 9-hydroxyphenanthrene (beta = 2.800, 95 % CI: 0.900, 4.701), and total OH-PAHs (beta = 0.073, 95 % CI: 0.028, 0.119). Logistic regression indicated that 3-hydroxyfluorene exposure was strongly associated with increased odds of overweight (adjusted OR = 12.66, 95 % CI: 2.94-54.54). Mixture analyses using G-computation (g-comp) and generalized weighted quantile sum (gQWS) regression confirmed the overall positive effect of PAH mixtures on child weight (beta = 0.425 and 0.285, respectively; p < 0.01), though associations with BMI were weaker and non-significant. Bayesian kernel machine regression (BKMR) further highlighted dose-response relationships for weight but not BMI. These findings suggest that prenatal PAH exposure may contribute to increased weight and risk of overweight in early childhood, emphasizing the need for public health interventions to reduce maternal exposure to PAHs during pregnancy. https://doi.org/10.1016/j.ecoenv.2025.119022

Per- and poly-fluoroalkyl substances exposure and risk of gastrointestinal cancers: a systematic review and meta-analysis,
Zhang, S. R., Kappil, E. M., Zheng, T. Z., Boffetta, P. and Seyyedsalehi, M. S., *European Journal of Cancer Prevention*, Sep 2025, Vol. 34, no. 5, p. 445-455.

BackgroundPer- and poly-fluoroalkyl substances (PFASs) are a group of synthetic chemicals used since the 1940s in industrial and consumer applications. These substances are known or suspected to cause cancer, particularly kidney and testicular cancer. However, their association with other types of cancer is not well understood. This review aims to investigate the link between PFAS exposure and the risks of other cancers, including gastrointestinal cancers such as esophageal, gastric, colorectal, and pancreatic cancer. Methods We conducted a systematic review of literature from the International Agency for Research on Cancer Monographs, Agency for Toxic Substances and Disease Registry documents, and PubMed (up to January 2024) focusing on the association between PFAS exposure and gastrointestinal cancers. Four independent reviewers screened the studies, extracted the information, and evaluated the quality of the studies using a modified Newcastle-Ottawa Scale. Meta-analyses were performed with random-effects models, including stratified analyses and dose-response assessments. Results The meta-analysis included 17 studies. The summary relative risks (RR) of esophageal cancer for perfluorooctanoic acid (PFOA) exposure was 0.75 (95% confidence interval [CI], 0.35-1.60; n = 2), and for perfluorooctane sulfonic acid (PFOS) was 1.76 (95% CI, 0.32-9.68; n = 1). The RR for gastric cancer and PFOA was 0.59 (95% CI, 0.28-1.21; n = 2) and PFAS was 0.96 (95% CI, 0.83-1.12; n = 2). The RR for colorectal cancer and PFOA was 0.83 (95% CI, 0.65-1.06; n = 6) and PFOS was 0.71 (95% CI, 0.22-2.27; n = 4). The RR for pancreatic cancer was 1.02 (95% CI, 0.90-1.15; n = 9) and PFOS was 0.92 (95% CI, 0.76-1.11; n = 2). Stratified analyses by geographical region, study design, quality score, year of publication, gender, and outcome revealed no associations for colorectal and pancreatic cancers. No dose-response trends were identified. Publication bias was suggested for gastric cancer. Conclusion Our study suggested no association between PFAS exposure and esophageal, gastric, colorectal, or pancreatic cancer. More rigorous research is needed to investigate this relationship in different settings, with precise PFAS quantification, a wider range of compounds, larger sample sizes for specific cancers, and better control for potential confounders. Our meta-analysis suggests inconclusive evidence, highlighting the need for further research. https://doi.org/10.1097/cej.0000000000000935

Sex-specific associations between phthalate exposure and stroke risk: a cross-sectional study integrating molecular mechanisms of vascular dysfunction,
Zhou, H.-Q., Cheng, K.-L., Jin, H.-J., Shen, J. Z. and Wu, D.-H., *International Journal of Surgery (London, England)*, 2025/11/10/ 2025.

BACKGROUND: Stroke is a significant global health issue, resulting in substantial mortality and morbidity. Environmental exposures are increasingly recognized as essential contributors to cerebrovascular risk profiles. Phthalates are ubiquitous synthetic plasticizers with well-established endocrine-disrupting properties and have been associated with various vascular and metabolic disturbances. However, their specific contribution to stroke pathogenesis, particularly concerning potential sex-specific vulnerability patterns, remains poorly understood. METHODS: A cross-sectional analysis was conducted on 8,184 participants (4,140 women and 4,044 men) from the National Health and Nutrition Examination Survey (NHANES) to evaluate the associations between urinary phthalate metabolite concentrations and stroke prevalence. The weighted quantile sum (WQS) regression methodology assessed the effects of cumulative exposure to the phthalate mixture. An integrative approach was used, incorporating network toxicology, protein-protein interaction mapping, and the Friends algorithm, to identify molecular targets related to stroke that may be affected by phthalate exposure. Molecular docking analyses were performed to characterise binding affinities between key phthalate metabolites and identified protein targets. We analyzed single-cell RNA sequencing data to determine cell-type-specific expression patterns of implicated molecular targets. RESULTS: Sex-stratified analyses revealed that phthalate exposure was positively associated with stroke risk in women but not in men. Specifically, higher urinary concentrations of Mono(carboxynonyl) phthalate (MCNP) were significantly associated with self-reported stroke in women. WQS regression confirmed cumulative effects, with MCNP identified as the primary contributor. Network and docking analyses revealed strong interactions between MCNP and vascular proteins KDR, AKT1, and MAPK8, which were predominantly expressed in endothelial cells. These findings suggest that phthalate exposure may increase stroke risk in a sex-specific manner through disruption of an endothelial-specific KDR-AKT1-MAPK8 signaling pathway. CONCLUSION: This work highlights a novel mechanism of environmentally mediated cerebrovascular risk and provides potential targets for therapeutic intervention, particularly in women.
https://doi.org/10.1097/JS9.0000000000003762

Hallmarks of EDCs among children in Southern China in Relation with obstructive sleep apnea, Zhou, L. X., Wang, S. H., Li, D. C., Li, J. H., Wang, X. Y., Zhong, S. Y., Li, X. J., Huang, S. Y., Zeng, C. Y., Duan, T. T., Wu, Y., Qi, G. L., Jing, F. R., Gong, Y. J., Yang, P. and Cheng, H. R., *Environment International*, Oct 2025, Vol. 204.

Childhood obstructive sleep apnea (OSA) is a common pediatric sleep disorder characterized by recurrent sleep-related upper airway dysfunction. China has the highest number of OSA sufferers (176 million) globally. Environmental endocrine-disrupting chemicals (EDCs) posed unrecognized threats to pediatric OSA are not clear. We examined the associations of 34 kinds of EDCs with childhood OSA in Southern China. We recruited 334 children aged <= 15 years (July-September 2022) from a tertiary sleep clinic in Shenzhen. Using HPLC-MS/MS, we quantified 7 organophosphate flame retardants (OPFRs), 3 parabens, 10 phthalate metabolites (PAEs), 4 benzophenones (BPs), 7 synthetic phenolic antioxidants (SPAs), and 3 bisphenols. Multivariable linear regression evaluated single-chemical associations with polysomnography-derived indices: apnea-hypopnea index (AHI), obstructive AHI (OAHI), oxygen desaturation index (ODI), and blood oxygen saturation (SpO(2)) levels. Mixture effects were assessed through quantile-based g-computation (Qgcomp). Multiple EDCs demonstrated significant dose-response relationships with AHI, OAHI, and ODI ($p < 0.05$), while inversely associated with SpO(2). Qgcomp revealed each tertile increase in EDC mixture concentration corresponded to elevated AHI [18.53 % (95 % CI: 6.18 to 32.31)], OAHI [23.27 % (13.88 to 34.99)], and ODI [15.03 % (5.13 to 24.61)], along with decreased baseline SpO(2) [-0.25 (-0.49 to -0.01)], lowest SpO(2) [-1.09 (-2.17 to -0.01)], and mean SpO(2) [-0.39 (-0.70 to -0.07)], with DBP exhibiting the strongest negative effects on AHI, OAHI, and ODI, and BCIPP showing the

greatest positive effects on baseline and mean SpO(2). This first biomonitoring study implicates EDC mixtures, particularly phthalates and OPFRs, in pediatric OSA pathogenesis. Our findings underscore the need for chemical policy reforms and longitudinal investigations elucidating biological mechanisms linking environmental exposures to sleep-disordered breathing. https://doi.org/10.1016/j.envint.2025.109829

Toxicité sur l'homme

The impact of perfumes and cosmetic products on human health: a narrative review, Alblooshi, S., *Frontiers in Toxicology*, Aug 29 2025, Vol. 7.

Background The use of perfumes and cosmetic products is widespread, serving personal hygiene, aesthetic, and olfactory functions. However, concerns have been raised regarding the potential health impacts associated with long-term exposure to various ingredients used in these products.Objectives This narrative review aims to synthesize evidence on the health risks associated with perfumes and cosmetics, focusing on specific health concerns, including fertility, respiratory health, cancer risk, allergies, skin disorders, endocrine disruption, and neurological effects. It also discusses the presence of heavy metals in cosmetics, regulatory challenges, and the need for transparency in ingredient disclosure.Methods A comprehensive review of the literature that was published between 2005 and 2024 was conducted, examining findings from interdisciplinary studies relevant to the health impacts of cosmetic and fragrance products. The review highlights health concerns linked to specific chemical components, including synthetic chemicals such as phthalates, parabens, and volatile organic compounds (VOCs).Results The findings indicate that many synthetic chemicals in perfumes and cosmetics are associated with adverse health outcomes. These include allergies, respiratory issues, endocrine disruption, reproductive problems, and potentially cancer. Heavy metals in cosmetics also pose significant health risks. Despite regulatory guidelines, the cumulative and long-term effects of combined exposure to multiple cosmetic ingredients remain poorly understood and inadequately addressed.Conclusion There is a pressing need for stricter regulatory oversight and improved transparency in ingredient disclosure to safeguard consumer health. Further research is required to clarify the long-term health risks associated with the daily use of cosmetic products and to develop safer alternatives. https://doi.org/10.3389/ftox.2025.1646075

Effect of Dietary Exposure to Low-Density Polyethylene Microplastics and Their Potential Role as Estrogen Vectors In Vivo, Al-Jandal, N., Saheb, A. I., Alkhubaizi, A., Akbar, A., Al-Hasan, E., Hussain, S. and Al-Mansour, H., *Current Issues in Molecular Biology*, Aug 30 2025, Vol. 47, no. 9.

Microplastics (MPs) are a growing environmental concern due to their ability to adsorb hazardous chemicals, such as estrogens, and be ingested by marine organisms. This study focuses on low-density polyethylene (LDPE), a polymer widely used in Kuwait, to assess its role as a carrier of endocrine-disrupting chemicals (EDCs), specifically estrogens. Biological effects were evaluated using biomarkers such as cytochrome P450 1A (CYP1A) and vitellogenin (Vtg) gene expression. Virgin LDPE MPs were exposed to influent and effluent from a wastewater treatment plant (WWTP) for four weeks to facilitate estrogen absorption. The MPs were then incorporated into fish feed pellets for dietary exposure experiments. Fish were divided into three treatment groups-exposed to either virgin MPs, WWTP-influent MPs, or WWTP-effluent MPs-and monitored over four weeks. The results showed that WWTP-exposed MPs carried detectable levels of estrogen, leading to physiological effects on yellowfin bream. Fish in the control group, which received MP-enriched diets

without estrogen, experienced significant weight loss due to nutrient deprivation. In contrast, weight patterns in the treatment groups were influenced by estrogen exposure. The condition factor (CF) decreased across groups during the experiment but remained within acceptable health ranges. A significant reduction in the hepatosomatic index (HSI) was observed in the effluent-exposed group, likely due to lower estrogen levels reducing physiological stress. The findings confirm that LDPE MPs can act as carriers for estrogens, impairing fish growth and metabolism while disrupting biological processes such as cytochrome oxidase function. These results highlight the potential risks of MPs in marine ecosystems and underscore the need for further research to understand their long-term effects. https://doi.org/10.3390/cimb47090701

A Narrative Review of Heavy Metals and Sperm Quality: The Interplay with Antioxidant Imbalance and Reactive Oxygen Species,
Azil, S., Errafii, K., Benkhalifa, M., Louanjli, N., Ghazi, B. and Hamdi, S., *Current Issues in Molecular Biology*, Aug 13 2025, Vol. 47, no. 8.

Reproductive infertility is characterized by the inability to achieve pregnancy after a year or more of unprotected sexual intercourse. This review highlights the significant impact of exposure to both types of heavy metals (essential and non-essential) on the reproductive performance of various species, particularly humans. Heavy metals present a high atomic density and weight, including lead, mercury, cadmium, nickel, chromium, and arsenic, and are delivered into the environment through natural and human activities, posing a threat to ecological systems and human reproductive health. These heavy metals have the potential for bioaccumulation and can adversely affect male fertility and sperm quality due to their role in disrupting endocrine functions, altering hormone levels responsible for sperm production, and inducing oxidative stress. The elevated production of reactive oxygen species (ROS) exceeds the capability of antioxidants and can lead to the alteration of sperm quality. Seminal fluid contains antioxidants like vitamin C, vitamin E, zinc, and selenium to counteract the impacts of ROS and also to preserve the sperm function. This review aims also to explore the impact of heavy metals on sperm quality and their relationship with antioxidant imbalance and ROS. The exposure to heavy metals whether through occupational or environmental means increases the production of ROS and therefore leads to an imbalance of antioxidants production. All these factors have no doubt an impact on male reproductive health. https://doi.org/10.3390/cimb47080650

Prenatal exposure to Bisphenol-A as a risk factor for infant neurodevelopment,
Bello-Cortes, I. H., Garcia-Garcia, J. A., Gutierrez-Aguilar, M., Araiza-Olivera, D., Sánchez-Perez, C., Garcia-Cerón, G., Morán-Ramos, S., Tovar, H., Bonilla-Brunner, A. and Garcia-Arrazola, R., *Frontiers in Endocrinology*, Aug 29 2025, Vol. 16.

It has been established a chronic human exposure to a particular class of chemicals known as endocrine-disrupting compounds (EDCs). Studies conducted in vitro, in vivo, and in silico have demonstrated that EDCs can disrupt the endocrine system through epigenetic mechanisms. These changes can be heritable and are associated with a wide range of diseases. Since exposure concentrations of these compounds are measured in parts per million (ppm) or even parts per billion (ppb), a critical question arises: does this pose a significant risk to humankind and future generations? We conducted a comprehensive review of human epidemiological data to provide an assessment of the risk of neurodevelopmental disorders in children associated with maternal exposure to Bisphenol A (BPA). BPA is one of the most studied and relevant EDC's related to food exposure. Our analysis reveals a correlation between BPA exposure during pregnancy and behavioral issues in offspring on 80% of the reviewed articles. Notably, male infants exposed to BPA during the third trimester exhibited a heightened risk. Our findings highlight the importance of

considering potential new health regulations aimed at safeguarding the fetal environment and reducing the risk of neurodevelopmental disorders in children.
https://doi.org/10.3389/fendo.2025.1645540

Human Internal Exposures of Bisphenol A and Six Data-Poor Analogs Predicted by Physiologically Based Kinetic Models with Multimodal Parametrization,
Bigonne, H., Rolof, A., Potapova, I., Sturla, S. J. and Aichinger, G., *Environmental Science & Technology*, Oct 7 2025, Vol. 59, no. 39, p. 20919-20930.

Bisphenols (BP) AF, B, E, F, M, and S are increasingly used as bisphenol A (BPA) substitutes. Despite widespread exposure and potential adverse health outcomes, they are poorly understood in terms of toxicokinetics, i.e., their absorption, distribution, metabolism, and excretion. We thus developed physiologically based kinetic models for different human physiological standards to predict internal concentrations of prevalent bisphenols following oral exposure. To address the imbalances in available human data among these chemicals, we used multimodal parametrization methods, including in vitro measurements of metabolism, computational prediction of gastrointestinal absorption, and rat-human extrapolation of enterohepatic circulation. Then, the models were evaluated against available human toxicokinetic data for BPA and BPS, revealing that 66% of predicted C max, t max, and AUC values fell within a 2-fold difference from in vivo measures. Using environmentally relevant exposure levels to compare internal levels of all tested bisphenols, we observed significant differences in the toxicokinetic profiles. Concerning tissues of toxicological concern, BPS had the highest concentration in blood and testes, while BPM accumulated in the thyroid and BPAF in the breasts. The present models are expected to facilitate a more precise evaluation of health risks induced by BPA analogs, guiding their safer use.
https://doi.org/10.1021/acs.est.5c00513

Endocrine Disrupting Toxicity of Bisphenol A and Its Analogs: Implications in the Neuro-Immune Milieu,
Buoso, E., Masi, M., Limosani, R. V., Oliviero, C., Saeed, S., Iulini, M., Passoni, F. C., Racchi, M. and Corsini, E., *Journal of Xenobiotics*, 2025/02// 2025, Vol. 15, no. 1, p. 13.

Endocrine-disrupting chemicals (EDCs) are natural or synthetic substances that are able to interfere with hormonal systems and alter their physiological signaling. EDCs have been recognized as a public health issue due to their widespread use, environmental persistence and the potential levels of long-term exposure with implications in multiple pathological conditions. Their reported adverse effects pose critical concerns about their use, warranting their strict regulation. This is the case of bisphenol A (BPA), a well-known EDC whose tolerable daily intake (TDI) was re-evaluated in 2023 by the European Food Safety Authority (EFSA), and the immune system has been identified as the most sensitive to BPA exposure. Increasing scientific evidence indicates that EDCs can interfere with several hormone receptors, pathways and interacting proteins, resulting in a complex, cell context-dependent response that may differ among tissues. In this regard, the neuronal and immune systems are important targets of hormonal signaling and are now emerging as critical players in endocrine disruption. Here, we use BPA and its analogs as proof-of-concept EDCs to address their detrimental effects on the immune and nervous systems and to highlight complex interrelationships within the immune–neuroendocrine network (INEN). Finally, we propose that Receptor for Activated C Kinase 1 (RACK1), an important target for EDCs and a valuable screening tool, could serve as a central hub in our toxicology model to explain bisphenol-mediated adverse effects on the INEN.
https://doi.org/10.3390/jox15010013

Perturbateurs endocriniens et spermatogenèse,
C Sonigo, L. F.-G., *Réalités en Gynécologie-Obstétrique*, no. 226.

Les perturbateurs endocriniens sont des substances exogènes capables de perturber l'homéostasie hormonale, affectant ainsi la fonction de reproduction masculine. Ils peuvent en effet générer des anomalies au niveau de la spermatogenèse. L'objectif de cette étude est d'exposer l'impact des différents perturbateurs, tels que le bisphénol A, les phtalates, les pesticides, les substances per- et polyfluoroalkylées (PFAS), les dioxines, la pollution de l'air et les métaux lourds, sur la qualité du sperme et la fertilité masculine. Ces substances, via une exposition in utero ou à l'âge adulte, peuvent altérer la plupart des paramètres spermatiques (numération, concentration, mobilité et morphologie des spermatozoïdes). Ils peuvent également induire des dérégulations hormonales, des lésions des cellules testiculaires, des dommages de l'ADN spermatique et des risques accrus de malformations génitales. Face à ces enjeux, des efforts sont menés pour évaluer et réguler ces substances au niveau national et européen, notamment sous l'égide de l'ANSES. Le déclin croissant de la qualité du sperme souligne la nécessité de poursuivre les recherches, et de sensibiliser le public aux dangers des perturbateurs endocriniens. https://doi.org/, https://www.realites-pediatriques.com/wp-content/uploads/sites/6/2025/04/06_SONIGO_RGO.pdf

Environmental plastic pollutants and endocrine-related cancer: An updated view,
Cirillo, F., Sergi, V., Malaguarnera, R., Scordamaglia, D., Piro, S., Maggiolini, M., Lappano, R. and Francesco, E. M. D., *Ecotoxicology and Environmental Safety*, Oct 1 2025, Vol. 304.

Micro- and nano-plastics (MNPs) are debris generated from the fragmentation of larger plastic particles. Due to their pervasive and persistent nature, MNPs - accumulated in the environment and widespread distributed across diverse ecosystems - have been detected in human blood, tissues and cells. Once considered as biologically inert, MNPs are emerging as cellular stressors with acknowledged biological properties, leading to diverse physiopathological responses. Herein, we present the most recent findings regarding the actions of MNPs as endocrine disruptors, emphasizing the novel findings suggestive of a potential stimulatory role played by these environmental pollutants in hormone-related cancers. In this vein, we provide a critical overview of the molecular mechanisms and the metabolic pathways activated by MNPs and implicated in the disruption of hormone/hormone receptor signaling, possibly leading to cancer progression. Next, we highlight the main areas of knowledge gap in the field, suggesting novel approaches that may allow a better understanding of environmental MNPs' action in human diseases. Considering the escalating environmental exposure to MNPs envisaged for the next years, irrespective of any counteractive measure, our comprehensive and detailed analysis contributes to a better evaluation of the endocrine effects associated with these emergent environmental pollutants. Our work corroborates research efforts worldwide, helping to build and expand knowledge on the endocrine effects elicited by MNPs, also in hormone-related cancers.
https://doi.org/10.1016/j.ecoenv.2025.119077

Thyrotoxic effects of organophosphate insecticides in adults: a bibliometric and meta-analysis,
Diawara, M. O., Pan, G., Yang, X., Alqudaimi, M., Fofana, M., Bafei, S. E. C., Wu, D., Tun, H. M., Liu, Q., Zhang, M. and Xia, Y., *International Archives of Occupational and Environmental Health*, 2025/09/01/ 2025, Vol. 98, no. 7, p. 631-647.

Organophosphate insecticides (OPIs) are widely used worldwide, raising growing concerns over their potential thyrotoxic effects. Despite mounting evidence, inconsistencies persist regarding their impact on thyroid hormone (TH) regulation in humans. This study aimed to clarify the relationship

between OPI exposure and TH levels in adults, addressing a critical gap in environmental health research. https://doi.org/10.1007/s00420-025-02159-2

The Detrimental Impact of Bisphenol S (BPS) on Trophoblastic Cells and the Ishikawa Cell Lines: An In Vitro Model of Cytotoxic Effect and Molecular Interactions,
Drakaki, E., Mavrogianni, D., Potiris, A., Xydi-Chrysafi, S., Kotrotsos, P., Thomakos, N., Rodolakis, A., Daskalakis, G. and Domali, E., *Biomedicines*, Aug 8 2025, Vol. 13, no. 8.

Background/Objectives: Bisphenols (BPs) and especially bisphenol S (BPS), an analog of bisphenol A (BPA), are widely used and induce oxidative stress, resulting in the inhibition of cell proliferation and induction of apoptosis which all are crucial for reproduction, the progression of pregnancy, and fertility. The present study integrates trophoblastic cells as an in vitro model to provide evidence and investigate the molecular interactions regarding placenta-related pregnancy complications after cytotoxic exposure to BPS. Methods: Human endometrial epithelial adenocarcinoma Ishikawa cell lines and trophoblastic cells were cultured. Cells obtained from the cultures were divided into plates and incubated for 24 h with different concentrations of bisphenol S (BPS). Cell viability was measured using the Countess Automated Cell Counter and the viability of Ishikawa cells was assessed after 48 h and for trophoblasts after 24 h. The effect of siRNA on NANOG expression was evaluated using qRT-PCR. Quantification of DNMT and NANOG was performed by qPCR and the G6PD gene was used as an internal control. Results: Real-time PCR results showed that the expression of the DNMT1 gene varies depending on the concentration of BPS in trophoblastic cells. In Ishikawa cell lines, real-time PCR results showed that DNMT1 gene expression was higher due to cell increase, but the measured fold change did not differ significantly. Data analysis indicated a statistically significant difference between CpDNMT1 in trophoblasts with and without BPS, where higher values were observed in the case of BPS presence ($p = 0.019$). The largest difference was observed between CpDNMT1 trophoblasts without BPS and CpDNMT1 Ishikawa with BPS ($p < 0.001$). Silencing the NANOG gene resulted in a reduced expression of DNMT1, while the G6PD gene was still detected. Conclusions: The results of this study highlight the cytotoxic effects of BPS and consequently its effect on trophoblast viability. The results of NANOG-DNMT1 gene expression related to BPS exposure reinforces our understanding of EDC-induced placental dysfunction. https://doi.org/10.3390/biomedicines13081938

The Role of Endocrine Disrupting Chemicals in the Development of Atherosclerosis,
Fenercioglu, A. K. and Unal, D. O., *Cardiovascular Toxicology*, Nov 2025, Vol. 25, no. 11, p. 1706-1717.

Endocrine disrupting chemicals (EDCs) are exogenous compounds that interfere with the normal functioning of the endocrine system. This effect is crucial for maintaining hormonal balance and regulating various physiological processes. Phthalates, parabens, and triclosan are EDCs found in many personal care products (make-up, shampoo, perfume, shaving foam, moisturizing cream, hair dyes, deodorant), plastics, pesticides, pharmaceuticals, and household cleaning products, and can be inhaled or absorbed by the body through inhalation or skin contact. Atherosclerosis is a major cause of cardiovascular diseases, including coronary artery disease, stroke, and peripheral artery disease. While traditional risk factors for atherosclerosis, such as high cholesterol, hypertension, and smoking, have been extensively studied, emerging evidence suggests that EDCs may also play a significant role in the development and progression of atherosclerosis. Several potential mechanisms have been proposed to explain how EDCs contribute to atherosclerosis. One mechanism involves the activation of nuclear receptors, such as peroxisome proliferator-activated receptors (PPARs) and estrogen receptors (ERs), by EDCs. Activation of these receptors can lead to dysregulation of lipid metabolism, inflammation, and oxidative stress, all of which are key processes

in atherosclerosis development. EDCs have been shown to disrupt endothelial function through various mechanisms. Some of these mechanisms are the formation of reactive oxygen species (ROS) and free oxygen radicals, and impaired nitric oxide (NO) production by EDCs. This literature review aims to explore the current understanding of the role of EDCs in atherosclerosis. https://doi.org/10.1007/s12012-025-10054-y

Benzophenones: How ultraviolet filters can interfere with reproduction, Gomez, J. M. R., *Journal of Neuroendocrinology*, 2025.

Benzophenones (BPs) are widely used as ultraviolet (UV) filters in personal care products, plastics, and food packaging. Although they serve as effective photoprotective agents, growing evidence suggests that BPs can act as endocrine-disrupting chemicals (EDCs), interfering with hormone regulation and reproductive functions. This review summarizes the current knowledge on BP exposure, metabolism, and their potential effects on reproductive health. We discuss the mechanisms by which BPs interact with hormonal receptors, alter steroid metabolism, and influence the hypothalamic-pituitary-gonadal axis. Special attention is given to BP-2 and BP-3, which have been detected in human biological samples, including urine, blood, and fetal tissues. Additionally, we highlight recent findings from in vitro and in vivo studies demonstrating their estrogenic activity and potential impact on reproduction. The review also addresses regulatory concerns, emphasizing the need for stricter policies to limit human and environmental exposure to BPs. Understanding the effects of these chemicals is essential for assessing their safety and developing alternatives to mitigate potential health risks. https://doi.org/10.1111/jne.70088

PFBS disrupts lipid metabolism and mitochondrial function in human trophoblast cells, Happel, J., Mellouk, N., Crute, C. and Feng, L. P., *Toxicology*, Dec 2025, Vol. 518.

Perfluorobutanesulfonic acid (PFBS) is an emerging short-chain per- and polyfluoroalkyl substance (PFAS), a group of persistent environmental contaminants associated with adverse reproductive outcomes. The placenta plays a critical role in the pathogenesis of pregnancy complications, and disrupted placentation is implicated in the mechanistic pathways linking PFBS exposure to these disorders. In particular, placental mitochondria function refines during pregnancy to optimize the dynamic growth of the fetus and placenta. Disruptions in mitochondrial function may therefore mediate the adverse effects of environmental exposure on pregnancy outcomes. This study investigated the effects of PFBS on the metabolism and mitochondrial function of human syncytiotrophoblast (STB), the primary nutrient-transporting cells of the placenta. Using a human trophoblast stem cell model, we differentiated cells into STBs and exposed them to an environmentally relevant dose of PFBS (100 mu M) for 24 h. Transcriptomic (RNA-seq) analysis identified 22 downregulated genes and 10 upregulated genes (FDR < 0.05). Integrated transcriptomic and metabolomic analyses revealed that PFBS significantly disrupted lipid metabolism, notably downregulating PPARG, a key regulator of placental lipid homeostasis, and carnitine shuttle genes CPT1A and SLC25A20, which are essential for mitochondrial fatty acid import. Further functional assessments found increased mitochondrial DNA copy number, yet decreased ATP production, indicating mitochondrial dysfunction. However, PFBS exposure did not induce oxidative stress nor alter mitochondrial morphology. These findings demonstrate that PFBS induces metabolic toxicity in human STBs, primarily by disrupting lipid metabolism and mitochondrial energy production. This mechanism may underlie the observed associations between PFBS exposure, placental dysfunction, and adverse pregnancy outcomes. https://doi.org/10.1016/j.tox.2025.154269

Liquid Crystal Monomers and Their Mixtures Alter Nuclear Receptor Signaling and Promote Adipogenesis In Vitro,
Heldman, S. M., Eccles, K. M. and Kassotis, C. D., *Endocrinology*, Nov 2025, Vol. 166, no. 11.

Liquid crystal monomers (LCMs) are ubiquitous environmental contaminants released from electronic devices' liquid crystal display (LCD) panels, which have led to the contamination of food, breast milk, and serum. As the toxicity of individual LCMs, not to mention their myriad mixtures, is currently very poorly characterized, there is a crucial need for investigations into the health hazards posed by exposure. In this study, 10 nonfluorinated (NF) and fluorinated (F) LCMs and 3 fluorination-based LCM mixtures were screened for metabolism and endocrine-disrupting potential in vitro at exposure-relevant concentrations using adipogenesis assays and luciferase reporter gene assays. Both NF-LCMs, F-LCMs, and their mixtures were found to alter the transcriptional activity of one or more nuclear receptors. Notably, 6 LCMs and all LCM mixtures were able to antagonize the progesterone receptor, with several displaying non-monotonic concentration-response curves. Multiple LCMs and their mixtures also increased triglyceride accumulation in murine preadipocytes and human mesenchymal stem cells in a concentration-dependent manner. The concentration addition principle underestimated the adipogenic potencies of LCM mixtures when compared with those derived from benchmark concentration analyses of empirical adipogenesis assay results, suggesting synergistic interactions. While no mechanistic pattern emerged between the bioactivities, results confirmed the metabolism and endocrine-disrupting potential of both NF-LCMs, F-LCMs, and their mixtures. This emphasizes the need to further investigate the metabolic and reproductive health impacts of LCM exposure in vivo, as well as the necessity of exploring alternative models to predict the toxicity of LCM mixtures. https://doi.org/10.1210/endocr/bqaf143

Genomic evidence based on eQTL data implicates endocrine disruptors as environmental risk factors for estrogen receptor-positive breast cancer,
Hong, Y. G., Li, J. J., Du, Z. Y., Xu, N., Yang, Q. R., Zhou, J. X. and Shu, W. Y., *International Journal of Surgery*, Aug 2025, Vol. 111, no. 8, p. 5664-5674.

Background:Estrogen receptor-positive (ER+) breast cancer is the most common molecular subtype of breast cancer and is strongly influenced by hormonal and environmental factors. Endocrine-disrupting chemicals (EDCs), which interfere with hormone signaling, have been suggested to contribute to ER+ breast cancer risk, but causal mechanisms remain unclear.Methods:We integrated chemical-gene interaction data from the TEDX and CTD databases with large-scale genomic datasets to investigate the relationship between EDC-regulated gene expression and ER+ breast cancer. A total of 5797 EDC-related genes were identified and filtered using cis-expression quantitative trait loci (cis-eQTL) data from eQTLGen. Mendelian randomization (MR) and colocalization analyses were performed using ER+ breast cancer GWAS summary statistics to assess causal associations and shared genetic signals. Interacting EDCs were mapped to colocalized genes.Results:Among 4207 genes with available cis-eQTLs, 50 showed statistically significant associations (FDR < 0.05) with ER+ breast cancer. Of these, 24 genes, including CIRBP, JMJD1C, and TET2, demonstrated strong evidence of colocalization. Key EDCs, such as bisphenol A and phthalates, were identified to interact with multiple high-risk genes, suggesting potential environmental drivers of ER+ breast cancer.Conclusion:This study provides genetic evidence supporting the causal role of EDC-regulated gene expression in ER+ breast cancer. The integration of MR, colocalization, and chemical-gene networks offers a novel framework for identifying environmentally relevant risk factors and contributes to understanding the gene-environment mechanisms underlying hormone-dependent cancers.
https://doi.org/10.1097/js9.0000000000002642

Integrative causal and single-cell analyses reveal genes responsive to endocrine disruptors driving human male infertility,
Hong, Y. G., Wang, Y. R., Li, J. J., Shu, W. Y., Chen, H. L. and Chen, C. D., *Ecotoxicology and Environmental Safety*, Sep 1 2025, Vol. 302.

Male infertility is a growing global health concern increasingly linked to environmental exposure to endocrinedisrupting chemicals (EDCs). However, the specific molecular mechanisms by which EDCs contribute to impaired reproductive function remain unclear. In this study, we systematically identified EDC-related genes using curated chemical-gene interaction databases and assessed their causal roles in male infertility through Mendelian randomization (MR) and colocalization analyses, utilizing large-scale cis-eQTL and GWAS datasets. A total of six genes, RHEB, PARP1, SLTM, PLIN1, PEX11A, and SDCBP, showed strong evidence of causal relationships and shared genetic variants associated with both gene expression and infertility traits. Single-cell RNA sequencing of human testicular tissue revealed that these genes are predominantly expressed in germ cells and are significantly dysregulated in non-obstructive azoospermia (NOA) samples, supporting their functional relevance. Additionally, environmental mapping indicated that several widely encountered EDCs, including bisphenol A (BPA) and its analogs, triphenyl phosphate (TPP), and sodium arsenite, interact with multiple candidate genes. These findings provide mechanistic insight into how chemical exposures can dysregulate gene expression in testicular cells and contribute to male infertility, highlighting the need for targeted environmental risk assessments and regulatory strategies. https://doi.org/10.1016/j.ecoenv.2025.118709

Microplastics and gynecological tumors: An emerging environmental health concern,
Hu, Y. L., Song, Z. H., Li, J. W., Yang, F. Y. and Li, L., *Reproductive Toxicology*, Oct 2025, Vol. 137.

The pervasive environmental contamination by microplastics (MPs) has emerged as a significant threat to human health, with mounting evidence linking exposure to gynecological tumors. This comprehensive review synthesizes current scientific evidence by examining the established risks of chemical additives, exploring the carcinogenic mechanisms of the particles themselves, and highlighting the recent direct detection of MPs in human gynecological tissues. Evidence for this association is multi-faceted: plastic additives such as phthalates and bisphenol A (BPA) are epidemiologically linked to increased cancer risk, while the MP particles themselves are shown to induce pro-carcinogenic responses including oxidative stress, chronic inflammation, and epigenetic changes. Critically, recent studies now confirm the physical presence of MPs within human gynecological tumor tissues, often at higher concentrations than in adjacent normal tissue, strengthening the clinical relevance of these findings. The convergence of chemical, mechanistic, and clinical evidence establishes a compelling case for MP exposure as an emerging risk factor for gynecological malignancies. The findings underscore an urgent need for further research, standardized detection methodologies, and public health strategies to mitigate this environmental threat. https://doi.org/10.1016/j.reprotox.2025.109018

The relationship between PFAS exposure and dyslipidemia: an updated review, meta-analysis, and evaluation of bias,
Hussey, M. R., Kornberg, T. G., Sherrick, J. M., Olson, A. M., Kind, J. A. and Perez, A. L., *European Journal of Epidemiology*, Sep 2025, Vol. 40, no. 9, p. 995-1029.

There is concern that widespread exposure to per- and polyfluoroalkyl substances (PFAS) may induce changes in serum lipids, however, current evidence is insufficient to establish causality in humans. This systematic review evaluated 69 articles examining exposure to perfluorooctanoic acid (PFOA) or perfluorooctane sulfonic acid (PFOS) and alterations in adult serum lipid outcomes. The

majority of associations for PFOA or PFOS with serum lipids were either not significant, significantly negative, or were mixed versus significantly positive findings, suggesting non-consensus of any associations. A subset of 37 studies were examined via meta-analysis and reviewed for biases. Using pooled estimates, PFOA and PFOS exposure were significantly positively associated with total cholesterol (TC) and low-density lipoprotein (LDL). PFOA was significantly positively associated with triglycerides (TG), whereas PFOS had a non-significant positive association with high-density lipoprotein (HDL). TC and LDL estimates demonstrated high heterogeneity, peaking within cross-sectional and non-occupational studies that comprised the majority of the meta-analysis. Conversely, pooled estimates from longitudinal investigations trended towards null and were not significant. Potential reasons for heterogeneity were identified in a bias analysis and primarily included inconsistent confounding controls and possible subject recruitment bias from regions with known PFAS contamination. These factors indicate inconsistencies in PFAS-lipid literature that require further prospective investigations. https://doi.org/10.1007/s10654-025-01271-4

Tetramethyl Bisphenol F: Organ- and System-Specific Toxicity, Current Status, and Perspectives, Hwang, I., Cui, X. S. and Jeung, E. B., *International Journal of Molecular Sciences*, Sep 23 2025, Vol. 26, no. 19.

Tetramethyl bisphenol F (TMBPF) is being increasingly used as a Bisphenol A (BPA) substitute, particularly as a coating material for food and beverage cans. Unlike BPA, TMBPF is considered safe because of the lack of reported estrogenic effects, and it is often marketed under the "BPA-free" label. Initial cell-based assays and rat toxicity studies indicated much lower systemic and sex hormone-related toxicity of TMBPF compared with BPA, which has facilitated its substitution and significant market expansion. Since 2021, however, a growing body of research has reported various adverse effects of TMBPF across multiple biological systems. These include cytotoxicity associated with apoptosis and endocrine-disrupting effects on the thyroid axis, skeletal system, neurodevelopment, and reproductive function. Although the effects on the estrogen and androgen systems, as well as obesogenic potential, show variability across studies, several studies have indicated significant biological impacts. Of particular concern is the potential neurodevelopmental toxicity, which may manifest only after long-term exposure and is often irreversible. Even if current leaching levels from food contact materials are minimal, environmental accumulation and biomagnification over time may pose significant risks. Therefore, comprehensive toxicological profiling of TMBPF is essential. This review summarizes the current toxicological findings on TMBPF and discusses the implications for future research and regulatory considerations, highlighting the importance of early attention to potential public health impacts. Strengthening the toxicological evidence base will help inform regulatory frameworks and support proactive measures to safeguard consumer safety as the use of TMBPF expands. https://doi.org/10.3390/ijms26199280

Impact of nanoplastics on thyroid function: Unraveling cellular biokinetics, molecular mechanisms and human risk assessment,
Iglesias-Hernandez, P., Tarazona, J. V., Manosalva, J., Megias, D., Docando, F., Cañas-Portilla, A. I., Torres-Ruiz, M. and De La Vieja, A., *Journal of Hazardous Materials*, Oct 15 2025, Vol. 498.

Nanoplastics (NP) have emerged as a significant environmental and health concern with endocrine disrupting potential that remain largely unknown. This study investigates the effects of Polystyrene NP (PSNP) on thyroid disruption using thyroid-derived cell lines, focusing on cellular biokinetics, distribution, alteration of redox balance and impact on thyroid hormone (TH)-related gene and protein expression and function. PSNP were rapidly internalized in a cell-type-dependent manner and localized in lysosomes and the endoplasmic reticulum with limited clearance. They led to time and concentration-dependent alterations in key thyroid hormone-related transcripts (e.g. NIS,

MCT8), without overt cytotoxicity. Toxicity data were used to calculate a benchmark dose (BMD5) for NIS gene (Slc5a5) inhibition at 11 particles/cell (0.21 mu g/mL), suggesting a robust point of departure for thyroid bioactivity. Our study demonstrates that PSNP elevated ROS levels, reduced cellular iodide uptake, disrupted TH homeostasis and could contribute to thyroid diseases such as hypothyroidism and impaired neurodevelopment. Moreover, we have identified PSNP as endocrine disruptors (thyroid modality), supporting their urgent consideration in regulatory actions given the recent detection of similar particles in human tissues. Our study provides novel insights into the potential molecular impacts of NP on thyroid physiology, and it highlights the importance of integrating New Approach Methodologies for risk assessment of NP.
https://doi.org/10.1016/j.jhazmat.2025.139890

The Role of Endocrine Disruptors in Childhood Obesity: Unraveling the Obesogens,
Kapama, A., Stefanaki, C., Mastorakos, G. and Papagianni, M., *Hormone Research in Paediatrics*, 2025.

Background: Obesity is a disease, acknowledged by WHO, characterized as an epidemic in a worldwide range, particularly in Western countries. Childhood obesity, lately, has raised major concerns. Among the complex factors contributing to obesity, environmental factors, such as endocrine disruptors, are gaining attention as emerging contributors to obesity. Summary: Toxicants, such as bisphenol A, phthalates, perfluoroalkyl and polyfluoroalkyl substances, heavy metals, and pesticides, have been associated with increases in the incidence of obesity in human populations, animals, and cellular models. These EDCs, called obesogens, disrupt the endocrine system across multiple pathways. They influence appetite, promote inflammation, disrupt the ecology and function of the gut microbiome, and induce transgenerational epigenetic changes. At the cellular level, they act as agonists of peroxisome proliferator-activated receptor gamma, steroid, and aryl hydrocarbon receptors. Key Messages: Children are exposed to obesogens through multiple metabolic pathways, which contribute directly and indirectly to the development of obesity. Despite the increasing evidence, more studies are needed to identify additional obesogens and elucidate their mechanisms of action to minimize exposure to pediatric and adolescent populations. (c) 2025 S. Karger AG, Basel https://doi.org/10.1159/000545043

Systematic review and Integrated Approaches to Testing and Assessment (IATA) of PFOA and PFOS for endocrine disrupting effects based on the AOP framework,
Kim, D., Ji, S. and Park, K., *Environmental Analysis, Health and Toxicology*, 2025/09// 2025, Vol. 40, no. Special Issue, p. e2025s03-00.

Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) have been extensively used as surfactants, surface protectors, food packaging materials, and fire-retardants. Due to serious adverse effects on human and environment, they are now considered as legacy compounds. In this study, the effects of PFOA and PFOS on endocrine disruption were assessed using the Integrated Approaches to Testing and Assessment (IATA) methodology based on the adverse outcome pathway (AOP). PFOA/PFOS in vitro data for enzyme activities for steroidogenesis, hormone levels of 17β-estradiol and testosterone, receptor binding capacity, receptor transcriptional activation, cell proliferation and differentiation were collated and assessed to elucidate the association between the data with the human adverse outcomes. Multiple studies indicate that PFOA/PFOS alter enzyme activities, hormone levels, receptor transcription, and cell proliferation. Moreover, associations were found between in vitro data and human outcomes including semen quality, menarche, menopause, menstrual cycle, infertility, miscarriage, cancer, and birth weight. This study effectively links toxic mechanisms to human adverse outcomes of PFOA and PFOS. However, in vitro data based on the molecular initial events (MIEs) and key events (KEs) in AOP frame works are not enough and often

inconsistent for integrated assessment, which suggest that more data for endocrine disruption are required for clear and complete IATA of PFOA and PFOS. https://doi.org/10.5620/eaht.2025s03

The Endocrine-Disrupting Chemical Benzophenone-3 in Concentrations Ranging from 0.001 to 10 µM Does Not Affect the Human Decidualization Process in an In Vitro Setting,
Krausser, K., Howanski, J., Fink, B., Bauer, M., Fischer, F., Romanelli, F., Zenclussen, A. C. and Schumacher, A., *International Journal of Molecular Sciences*, Sep 24 2025, Vol. 26, no. 19.

Endocrine-disrupting chemicals such as benzophenone-3 (BP-3) can have severe consequences for human reproduction by affecting critical processes during pregnancy. To shed further light on potential harmful BP-3 actions, our current study addressed the impact of BP-3 on decidualization and trophoblast invasion. Decidualization was initiated in human endometrial stromal cells (THESC) upon treatment with a mixture of cAMP, progesterone, and estradiol. In parallel to hormonal treatment, the cells were exposed to different BP-3 concentrations ranging from 0.001 mu M to 10 mu M. The expression of decidualization and invasion markers was determined. Moreover, trophoblastic spheroids derived from JEG-3 cells were transferred to decidualized THESC after BP-3 exposure, and spheroid attachment and invasion were analyzed. Hormonal treatment successfully initiated decidualization in THESC, which was confirmed by increased prolactin levels and IGFBP1 and NCOA-3 mRNA expression. Notably, BP-3 exposure did not affect these markers. Furthermore, BP-3 changed neither THESC proliferation nor viability nor the frequency of cells expressing MMP2/9 or TIMP1/3. Trophoblastic spheroid attachment and outgrowth into THESC were not altered through any of the BP-3 concentrations applied. Our results do not provide evidence for an influence of BP-3 on the decidualization process and the capability of trophoblast cells to adhere and invade into endometrial stromal cells. https://doi.org/10.3390/ijms26199314

Transformation of Bisphenols by Gut Microbiota: Insights into Species-Specific Pathways and Toxicity Implications,
Lv, M. L., Chen, S. Q., Qin, H., Wang, Y. L., Liu, Y. N., Liu, R. Z., Chen, L. Q., Qu, G. B. and Jiang, G. B., *Environmental Science & Technology*, Aug 12 2025, Vol. 59, no. 31, p. 16227-16239.

The widespread use of bisphenols (BPs) in consumer products has raised significant concerns regarding their environmental fate and potential health impacts. The metabolic processes and transformation products (TPs) of BPs in vivo play a crucial role in determining their toxicological effects, with the gut microbiota serving as a key factor. However, studies on transformation of BPs by GM are scarce. In this study, we investigated the transformation of 21 BPs by six human gut bacterial strains in vitro. Among these, bisphenol A-glycerol methacrylate (Bis-GMA) was significantly transformed by different bacteria, and eight species-specific TPs were identified, including acetylated, ester-hydrolyzed, and palmitoylated products. In vivo studies further confirmed that Bis-GMA was converted into bisphenol A bis (2,3-dihydroxypropyl) ether (Bis-HPPP), the same product identified in vitro. Bis-HPPP exhibited a lower cytotoxicity than Bis-GMA in cytotoxicity assays. Furthermore, compared to Bis-HPPP, Bis-GMA induced more severe damage to human intestinal organoid function, including effects on apoptosis, cell proliferation, and the expression of key biomarkers. Overall, our findings provide valuable insights into the species-specific transformation of environmental contaminants by a human GM, highlighting the important role of microbial transformation in modulating toxicity of environmental pollutants.
https://doi.org/10.1021/acs.est.5c01820

Potential human health effects of per- and polyfluoroalkyl substances (PFAS) prevalent in aquatic environment: a review,
Mayilswami, S., Raval, N. P., Tomar, R., Sharma, S., Praveena, S. M., Kataria, N., Selvasembian, R., Shanmugam, S. R., Nath, R., Malakar, A., Dutta, S. and Mukherjee, S., *Environmental Science-Advances*, 2025.

The widespread incorporation of per- and polyfluoroalkyl substances (PFAS) in various daily-use items has garnered considerable attention regarding environmental and health hazards in the last decade. Among different categories of PFAS, a paradigm shift has occurred towards short-chain PFAS alternatives like GenX, ADONA, and F53B, driven by environmental considerations and regulatory changes. Exposure to PFAS can happen through consuming contaminated food and drink, inhaling contaminated dust, or skin contact with PFAS-containing objects. Furthermore, occupational exposure might result from manufacturing and firefighting operations employing fluorinated compounds. In humans and monkeys, perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) exhibit an increased affinity for plasma proteins. However, the exact extent of this affinity is still a matter of research. The buildup of PFOS in the liver might cause injury or dysfunction by interfering with its regular operation. Compared to other human tissues, the liver has been shown to accumulate higher amounts of PFOS. Although there is an absence of epidemiological studies on PFOS, a possible connection between the health disorder and elevated cholesterol levels has been established by many researchers. Considering the transition as a future environmental burden, this review aims to bring together ongoing research compilations on short-chain PFAS, delving into their persistence, prevalence, and bioaccumulative toxicity in aquatic environments and focusing on critical areas of research gaps. An extensive literature analysis assessed the relative abundance of short-chain compounds compared to their long-chain counterparts within aquatic ecosystems. US EPA has setup new guidelines specifically for drinking water for PFOA and PFOS compounds which is 4 ppt. Furthermore, this review highlights emerging regulatory measures being implemented worldwide to safeguard public health. These measures encompass a range of strategies, from the European Union's emphasis on banning certain manufacturing and production practices under the REACH regulations to establishing exposure limits and disposal protocols in the United States. https://doi.org/10.1039/d4va00405a

The Impact of Endocrine Disruptors on the Female Genital Tract Microbiome: A Narrative Review,
Moustakli, E., Grigoriadis, T., Potiris, A., Drakaki, E., Zikopoulos, A., Anagnostaki, I., Zachariou, A., Domali, E., Drakakis, P. and Stavros, S., *Life-Basel*, Jul 24 2025, Vol. 15, no. 8.

Background/Objectives: Endocrine disruptors (EDs) are xenobiotic chemicals that disrupt hormone signaling and homeostasis within the human body. Accumulative evidence proposes that EDs could affect systemic hormone balance and local microbial communities, including the female genital tract (FGT) microbiome. The FGT microbiome, and especially the vaginal microbiota, contributes significantly to reproductive health maintenance, defense against infection, and favorable pregnancy outcomes. Disruption of the delicate microbial environment is associated with conditions like bacterial vaginosis, infertility, and preterm birth. Methods: The present narrative review summarizes the existing literature on EDs' potential for changing the FGT microbiome. We discuss EDs like bisphenol A (BPA), phthalates, and parabens and their potential for disrupting the FGT microbiome through ED-induced hormone perturbations, immune modulation, and epithelial barrier breach, which could lead to microbial dysbiosis. Results: Preliminary evidence suggests that ED exposure-microbial composition changes relationships; however, robust human evidence for EDs' changes on the FGT microbiome remains scarce. Conclusions: Our review addresses major research gaps and suggests future directions for investigation, such as the necessity for longitudinal and mechanistic studies that combine microbiome, exposome, and endocrine parameters. The

relationship between EDs and the FGT microbiome could be critical for enhancing women's reproductive health and for steering regulatory policies on exposure to environmental chemicals. https://doi.org/10.3390/life15081177

Exploring the impact of endocrine disruptors on hormonal regulation and adipose tissue in health and obesity,
Nirenjen, S., Singh, S. A., Begum, R. F., Arun, E., Vellapandian, C. and Narayanan, J., *Journal of Endocrinology*, Jul 1 2025, Vol. 266, no. 1.

Endocrine disruptors (EDs) are exogenous substances that interfere with the endocrine system, leading to adverse health outcomes. These substances, prevalent in industrial pollutants, pesticides, plastics, and personal care products, significantly impact hormonal regulation and disrupt various physiological processes. This review explores the sources and health impacts of EDs, focusing on their interference with hormonal axes, fetal development, and adipose tissue function. It highlights underlying mechanisms such as epigenetic modifications and discusses strategies to reduce ED exposure. Recent research reveals that EDs affect estrogen, androgen, and thyroid hormone signaling, contributing to developmental, reproductive, and metabolic disorders. Their interference with hormonal regulation is linked to abnormalities during fetal development and obesity through altered adipogenesis-related gene expression. Mechanisms such as DNA methylation, hypoxia-inducible factor signaling, and histone modifications play pivotal roles in ED-induced disruptions. Addressing ED exposure requires a multifaceted approach, incorporating lifestyle changes and public health initiatives to mitigate risks. Continued research is essential to better understand their effects and develop effective strategies for reducing their impact. https://doi.org/10.1530/joe-24-0374

Serum levels of per- and polyfluoroalkylated substances and methylation of DNA from peripheral blood (vol 13, 1621495, 2025),
Omichessan, H., Dragic, D., Perduca, V., Truong, T., Polidoro, S., Kvaskoff, M., Cano-Sancho, G., Antignac, J. P., Baglietto, L., Mancini, F. R. and Severi, G., *Frontiers in Public Health*, Sep 2 2025, Vol. 13. https://doi.org/10.3389/fpubh.2025.1679534

The Plasticizer Dibutyl Phthalate (DBP) Impairs Pregnancy Vascular Health: Insights into Calcium Signaling and Nitric Oxide Involvement,
Quelhas, A. R., Mariana, M. and Cairrao, E., *Journal of Xenobiotics*, Aug 6 2025, Vol. 15, no. 4.

Dibutyl phthalate (DBP) is used as a plasticizer to enhance flexibility in several household products, cosmetics, and food-contact materials. Due to its harmful effects, DBP is restricted or banned in children's products and food items, particularly in Europe. Due to its endocrine disruptor properties and considering its ability to cross the placental barrier, it is imperative to study DBP's vascular effects in pregnancy, given the vulnerability of this period. Thus, this study investigated the potential effects of DBP on the cardiovascular system using umbilical arteries from healthy pregnant women. Specifically, the impact of DBP on the vascular reactivity after both rapid and 24 h DBP exposure was analyzed, as well as the contractility and the cell viability of vascular smooth muscle cells (VSMC). DBP did not exhibit overt cytotoxic effects on VSMCs, possibly due to its adsorption onto polystyrene surfaces, potentially limiting bioavailability. Interestingly, DBP induced vasorelaxation in a concentration-dependent manner. Although mechanistic insights remain to be fully elucidated, the results suggest the involvement of pathways associated with nitric oxide signaling and calcium handling. Overall, DBP exposure appears to modulate arterial tone regulation, which may have implications for vascular function during pregnancy. https://doi.org/10.3390/jox15040127

Cell-free circulating epigenomic signatures: Non-invasive biomarkers of pregnancy-related outcomes associated with plasticizer exposure,
Rajan, A. K., Mohanty, A., Swain, P., Tiwari, R., Gurjar, V., Srivasatava, R. K. and Mishra, P. K., *Reproductive Toxicology*, Oct 2025, Vol. 137.

Globally, plastics have revolutionized industrial and societal advancements, but their durability and low degradability have led to significant environmental pollution. Plasticizers, such as bisphenol A (BPA) and phthalates, are widely used to enhance the flexibility and durability of plastics; however, they are also recognized as endocrine-disrupting chemicals (EDCs) with severe health implications. These chemicals are associated with reproductive toxicity, developmental disruptions, and multigenerational health effects. Recent research has highlighted the impact of plasticizers on irreversible epigenetic modifications, which influence abnormal gene expression patterns without altering the DNA sequence. Histone alterations, DNA methylation, and non-coding RNA regulation are essential pathways. Exposure to BPA and phthalates disrupts these epigenetic processes, leading to long-term reproductive health issues, including infertility, implantation failures, preterm birth, and pregnancy complications such as gestational diabetes and preeclampsia. Cell-free circulating nucleic acids are promising non-invasive biomarkers for the early detection of pregnancy complications, such as preeclampsia, with the potential to predict sensitivity and track gestational age and underlying pathophysiological processes. Combining circulating nucleic acid analysis with evaluations of plasticizer exposure may aid in stratifying highrisk pregnancies. Here, we examined the mechanisms by which plasticizers induce epigenetic alterations, their impact on reproductive health and pregnancy outcomes, and potential biomarkers for identifying these changes to facilitate tailored management of pregnancy complications and assess reproductive health risks.
https://doi.org/10.1016/j.reprotox.2025.109000

Bisphenol A Interferes with Mast Cell-Mediated Promotion of Cellular Processes Critical for Spiral Artery Remodeling,
Romanelli, F., Zhang, N. J., Bauer, M., Fink, B., Zenclussen, A. C., Schumacher, A. and Meyer, N., *International Journal of Molecular Sciences*, Oct 5 2025, Vol. 26, no. 19.

Mast cells (MCs) belong to the cell network that regulates uterine spiral artery remodeling (uSAR), a critical vascular adaptation supporting placental development and fetal growth. Our previous in vitro study demonstrated that human MCs promote trophoblast invasion, as well as uterine vascular smooth muscle cells (uVSMCs) migration and transition to a synthetic phenotype-essential steps for a successful uSAR. Although MCs are known targets of bisphenol A (BPA), a widespread endocrine-disrupting chemical, its impact on their supportive role in uSAR is unknown. In this study, we used murine cell lines to investigate whether BPA (0.1-100 mu M) affects MC-mediated promotion of cellular processes critical for uSAR. Our results showed that BPA exposure hindered MCs' ability to promote trophoblast invasion and the switch in uVSMCs' synthetic phenotype and migration. The highest concentrations of BPA altered the expression of genes related to MCs activation and proliferation, and of those involved in trophoblasts invasion. In contrast, low doses induced the expression of pro-inflammatory mediators in MCs without detectable effect on trophoblasts at the transcriptional level. These findings confirmed MCs as key mediators of uSAR, and identified BPA as a disruptor of their function, emphasizing its potential harmful impact on reproductive health.
https://doi.org/10.3390/ijms26199706

Exploring the Antagonistic Effects of Bisphenols with Nonmonotonic Dose-Response Curves on the Estrogen Receptor,
Su, J. H., Yang, X. X., Wang, D. Y., Liu, H. A., Kuang, Z. C., Liu, Q. S., Zhou, Q. F. and Jiang, G. B., *Environment & Health*, 2025.

The nonmonotonic dose-response curve (NMDRC) is a prevalent characteristic of endocrine-disrupting chemicals (EDCs) in activating nuclear receptors (NRs), implicating intricate regulatory mechanisms. In this study, the agonistic and antagonistic activities of 11 bisphenols on the estrogen receptor (ER) were screened using MVLN cells. Three distinct dose-response patterns were observed, namely, S-shaped, inverted S-shaped, and bell-shaped profiles, corresponding to the agonistic, antagonistic, and nonmonotonic effects on ERs, respectively. To further explore NMDRC, bisphenol B (BPB) and bisphenol AF (BPAF), as representative compounds, were specifically investigated for their antagonistic effects on ER under high exposure concentrations (10-50 mu mol/L). Notably, the successive decline in cell viability suggested a subhealthy cell state upon high-dose chemical treatments, compromising cell response in ER transactivation. Unlike the specific effect induced by an ER alpha antagonist (4-hydroxytamoxifen, 4OHT), the nonspecific inhibitory effects of BPB and BPAF on ER transactivation were further confirmed with their identical antagonistic curves, with or without E2 cotreatment, due to hydrophobicity-related cellular baseline toxicity. Accordingly, the inhibitory effects on NR transactivation might not necessarily be considered as a specific antagonistic activity. Thus, a more cautious inspection is highly encouraged in screening NR antagonism-centered endocrine-disrupting effects of emerging chemicals by carefully reviewing the specificity of signal reduction or inhibition. https://doi.org/10.1021/envhealth.5c00173

Endocrine disruption to metastasis: How phthalates promote breast carcinogenesis,
Tiburcio, D., Parsell, M., Shapiro, H., Adolphe, S., Naranjo, O., George, S. and Toborek, M., *Ecotoxicology and Environmental Safety*, Sep 15 2025, Vol. 303.

Breast cancer is a leading cause of death in women worldwide. Data suggests that hereditary factors only account for 5-10 % of breast cancer incidence, resulting in increased concern regarding the carcinogenicity involved with environmental and lifestyle-related factors. Among these, phthalates - ubiquitous endocrine disrupting chemicals founds in plastics, cosmetics, and food packaging - pose a growing concern. Human exposure to phthalates occurs through ingestion, inhalation, dermal contact, and critical windows such as intrauterine development. As an endocrine-responsive organ, the breast is particularly susceptible to disruption by these compounds. This review highlights emerging evidence linking phthalate exposure to the initiation, progression, and metastasis of breast cancer. This comprehensive overview of carcinogenesis-promoting mechanisms of phthalates, involving estrogen receptor signaling, oncogenic pathway activation, promotion of cancer stemness, and induction of therapy resistance, will provide crucial insights into phthalate-driven mechanisms in breast cancer that can inform future research directions, public health strategies, and regulatory efforts aimed at mitigating environmental cancer risks. https://doi.org/10.1016/j.ecoenv.2025.118874

Molecular Mechanisms of EDC-Induced Alzheimer's Disease and of Traditional Chinese Medicine Active Substances in Treating AD and Antagonizing EDC-Induced Effects,
Yang, T., *Neurochemical Research*, Oct 6 2025, Vol. 50, no. 5.

AD, a progressive neurodegenerative disorder, imposes an increasingly heavy burden on global public health, with its pathogenesis remaining incompletely understood. Meanwhile, EDCs-widely present in the environment, food, and consumer products-have emerged as a significant public health concern due to their diverse health risks, including potential contributions to

neurodegenerative processes such as AD by disrupting neurohomeostasis. Furthermore, as natural compounds, ginsenosides and other AS have been the focus of numerous studies exploring their role in treating AD, thanks to their advantages of multi-target properties and low side effects. However, the specific molecular pathways through which EDCs induce AD, as well as the mechanisms by which AS may counteract EDC-induced toxicity and intervene in AD, remain unclear. Against this background, this study sought to: (1) explore the molecular pathways through which EDCs may induce AD by disrupting neurohomeostasis; (2) preliminarily investigate the potential of AS in treating AD and antagonizing EDC-induced AD at the molecular level. To achieve these goals, we integrated network toxicology, network pharmacology, and molecular docking to construct a multi-dimensional interaction network among EDCs, AD, and AS. By establishing intersecting target sets for EDCs-AD and AS-AD, core targets were identified via topology analysis of protein-protein interaction (PPI) networks. GO and KEGG enrichment analyses highlighted key pathways, including serotonergic synapse and neuroactive ligand-receptor interaction. Molecular docking further explored interactions between EDCs/AS and core target proteins. The results suggest that EDCs may drive neurodegeneration in AD by impairing synaptic function, while AS may counteract these effects by enhancing synaptic activity, stabilizing membrane microenvironments, inhibiting A beta aggregation, alleviating neuroinflammation, and restoring metabolic homeostasis. Further analysis indicated that AS exhibit stronger binding ability to core targets compared to EDCs, implying a potential antagonistic effect of AS against EDCs. This study provides insights into the molecular mechanisms underlying EDC-induced AD and establishes a multi-target theoretical framework for AS-mediated antagonism of EDC toxicity, offering a reference for the prevention and treatment of neurodegenerative diseases. https://doi.org/10.1007/s11064-025-04570-0

Per- and poly-fluoroalkyl substances (PFAS) and human health: a review of exposure routes and potential toxicities across the lifespan,
Yeoh, C. S. L., Alrazihi, L. A., Wong, S. T. and Wong, S. F., *Environmental Toxicology and Chemistry*, Oct 2025, Vol. 44, no. 10, p. 2754-2786.

Research on toxicity, removal, and degradation of per- and polyfluoroalkyl substances (PFAS) has increased tremendously in the number of publications in recent years. The aim of this review was to summarize the source, exposure route, and potential toxicological effects of PFAS to humans. Relevant articles published between 2010 and 2022 were selected from PubMed and Scopus on the PFAS occurrence, exposure route, and potential toxicity effects on human health. This review discusses the potential exposure pathways to PFAS across various life stages, including contaminated food, drinking water, breastfeeding, indoor or outdoor air, and PFAS-containing consumer products. Furthermore, this paper highlights the possible associations between PFAS exposure and various health effects, and the mechanisms underlying these toxicological effects, including immune dysregulation and respiratory impacts, endocrine system disruptions (thyroid and pancreatic functions), lipid and metabolic dysregulation, systemic toxicities affecting the liver, cardiovascular system, and kidneys, as well as adverse reproductive and developmental outcomes, and the nervous system. https://doi.org/10.1093/etojnl/vgaf172

Polycystic ovary syndrome and organochlorine pesticides: exploring potential links and mechanisms,
Yin, S. S., Yang, W. J., Lin, F. Y., Jia, M., Feng, Y., Chen, Y. H., Bai, X. X., Dong, Y. H., Mao, S. D., Hayat, K. and Jin, X. J., *Frontiers in Reproductive Health*, Sep 2 2025, Vol. 7.

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder among women, characterized by metabolic abnormalities and infertility. Despite its high prevalence, the etiology and pathogenesis of PCOS remain poorly understood. Emerging evidence suggests that persistent organic pollutants

(POPs), known for their detrimental effects on the endocrine and reproductive systems, may play a role in the development and progression of PCOS. Among POPs, organochlorine pesticides (OCPs) are particularly widespread and pose significant health risks. This review examines the potential of OCPs as an environmental factor in the development and progression of PCOS. It highlights the mechanisms through which OCPs may disrupt the hypothalamic-pituitary-ovarian (HPO) axis and impair hormonal regulation, contributing to the onset and exacerbation of PCOS. Evidence links OCPs to insulin resistance, obesity, and type 2 diabetes mellitus. These disruptions may occur via pathways involving hypothyroidism or altered adrenal androgen secretion. While current evidence supports a plausible connection between OCP exposure and PCOS, significant gaps and inconsistencies in the data warrant further investigation. Elucidating the precise mechanisms underlying these associations is crucial for developing targeted prevention and intervention strategies. https://doi.org/10.3389/frph.2025.1563414

Effects of an environmentally relevant mixture of organophosphate esters on the phenotype and function of HepG2 liver cells,
Yu, D. W., Hales, B. F. and Robaire, B., *Archives of Toxicology*, Dec 2025, Vol. 99, no. 12, p. 5005-5022.

Organophosphate esters (OPEs), commonly used as flame retardants and plasticizers, are ubiquitous environmental contaminants, with high concentrations found in indoor house dust. Previously, we have reported that individual OPEs have adverse effects on HepG2 liver cells. However, real-world exposure involves mixtures of OPEs. In this study, we investigated the effects of an environmentally relevant mixture of OPEs, detected in Canadian house dust, on HepG2 cell phenotype and function. Using high-content imaging, we found that this mixture increased cytotoxicity and lipid droplet size, while lysosomes were the most effected endpoint. We used the DQ-BSA degradation assay to assess the function of lysosomes and confocal microscopy to confirm the status of lysosomal transcription factor EB (TFEB). We then tested lysosomal enzyme activities to determine potential downstream effects. OPE mixture induced concentration-dependent increases in the degradation capacity of lysosomes and elevated nuclear translocation of TFEB when compared to controls. Increased activities of downstream lysosomal acid lipase (LAL) and cathepsin B (CTSB) validated the activation of TFEB and its downstream effect of lysosome biogenesis. Together, these data demonstrate that exposure to an environmentally relevant OPE mixture adversely affects liver cell survival, phenotype, and lysosome functions, providing potential mechanistic insight into consequences of OPE exposure and increased risk of liver damage associated with disrupted lipid and lysosome homeostasis. This study also highlights the importance of evaluating real-world chemical exposures as mixtures rather than as individual compounds. https://doi.org/10.1007/s00204-025-04173-2

Transgenerational hepatotoxicity induced by bisphenol B as a substitute for bisphenol A,
Yue, H. F., Hu, Y. C., Wu, X. Y., Tian, Y. C., Liang, X. M., Zhang, J. Y., Li, B., Zhu, H. Z. and Ji, X. T., *Ecotoxicology and Environmental Safety*, Sep 1 2025, Vol. 302.

Accumulating evidence identifies bisphenol A (BPA) as an endocrine disruptor with demonstrated hepatotoxicity, driving the adoption of structural analogs like bisphenol B (BPB). Pregnancy constitutes a critical developmental window for endocrine disruptor-mediated hepatotoxicity in offspring. However, systematic toxicity evidence about BPB exposure-induced transgenerational hepatotoxicity in offspring remains scarce, and the regulatory mechanisms need to be further explored. To elucidate the gene markers and signaling pathways involved in the developmental origins of liver dysfunction induced by direct/maternal BPB exposure. In this study, we systematically analyzed the mechanism of hepatotoxicity and transgenerational effects of BPB by

animal models (BPB, direct exposure and maternal exposure, 300 mu g/kg bw (body weight)/day). Biochemical indicators and histopathological changes were examined, and bioinformatics analysis was used to explain the relationship between BPB exposure and the liver injuries. The results showed that direct BPB exposure induced subclinical hepatotoxicity with significant cholesterol reduction, circadian rhythm disruption, and Tmem87b/ Fkbp1a-mediated chemoresistance. Maternal BPB exposure caused offspring hepatomegaly, transaminase elevation, drove oxidative stress and lipid metabolism imbalance through the Ppard-Slc23a2 dysregulation. Bioinformatics validation in human hepatocellular carcinoma (HCC) confirmed prognostic significance of Tmem87b/Fkbp1a/Ppard/Slc23a2. The study confirmed that BPB induces hepatotoxicity through circadian disruption and oxidative stress pathways, establishing these genes as dual biomarkers for early detection and therapeutic response prediction. https://doi.org/10.1016/j.ecoenv.2025.118702

Exposure to Bisphenol B and S Increases the Risk of Male Reproductive Dysfunction in Middle Age,
Zhao, S., Ni, H. L., Xiao, Y., Du, J., Han, Y. D., Wang, W. Y., Tang, S. and Yu, M. X., *International Journal of Molecular Sciences*, Sep 28 2025, Vol. 26, no. 19.

Accumulating evidence indicates that bisphenol A (BPA) analogs, including bisphenol B (BPB) and bisphenol S (BPS), disrupt testicular function and contribute to male reproductive dysfunction (MRD). However, whether BPA analogs are involved in MRD among middle-aged men remains inconclusive. Therefore, we selected cryptorchidism, erectile dysfunction, premature ejaculation, and testicular tumors as representative MRD conditions in middle-aged individuals, aiming to explore the molecular mechanisms that may be disrupted by bisphenols (BPs). By using GeneCards, STRING and Cytoscape, TP53, AKT1, and MYC were pinpointed as core targets associated with MRD. Enrichment analysis suggested that BPs may induce MRD by disrupting steroidogenesis. UPLC-MS/MS analysis showed that both BPB and BPS exhibit specific accumulation in the testes. Following 20-day exposure to 0.3 or 0.6 mg/kg body weight/day BPB or BPS, testosterone levels and the expression of hub genes were decreased. The molecular docking results demonstrated that both BPB and BPS can directly bind to members of the cytochrome P450 family, potentially interfering with sex hormone biosynthesis. Our study identified the targets and mechanisms through which BPB and BPS induce MRD in middle-aged males, thereby providing insights for the safety assessment of BPs. https://doi.org/10.3390/ijms26199507

Environmental Endocrine-Disrupting Chemicals, Pancreatic β-Cells, and Type 2 Diabetes Mellitus, Zhao, Y. L. and Ou, Y., *Clinical Endocrinology*, 2025.

Objective To clarify the link between environmental pollution and diabetes risk by focusing on pancreatic beta-cells as key targets of environmental insults, with emphasis on the role of endocrine-disrupting chemicals (EDCs) in pancreatic dysfunction and diabetes pathogenesis.Methods This narrative review synthesises recent research on EDCs, focusing on their effects on beta-cells. The literature search included studies in English on EDCs, diabetes, and beta-cell function, utilising Boolean operators to refine the search.Results EDCs impair beta-cell function through mechanisms such as oxidative stress, mitochondrial damage, and epigenetic changes. These pollutants disrupt insulin synthesis, secretion, and beta-cell survival, which is distinct from their general metabolic effects. Additionally, EDCs may interact synergistically with traditional diabetes risk factors, such as high-fat diets, amplifying the risk of diabetes.Conclusion Environmental pollutants play a significant role in beta-cell dysfunction and diabetes, offering new directions for research and prevention. https://doi.org/10.1111/cen.70050

Mechanisms of three typical endocrine-disrupting chemicals causing myocardial infarction: Gene-level computational modeling,
Zhou, J. X., Chen, S. S., Zheng, Z. Y., Yuan, W. B., Liu, X. B. and Ni, H. G., *Environmental Chemistry and Ecotoxicology*, 2025 2025, Vol. 7, p. 1761-1773.

Endocrine disruptors chemicals (EDCs), as environmental pollutants, have been recognized as potential risk factors for myocardial infarction (MI), but the specific mechanism of action is still unclear. In this study, the molecular roles of three typical EDCs, i.e., bisphenol A (BPA), bis(2-ethylhexyl) phthalate (DEHP) and dichlorodiphenyltrichloroethane (DDT) in MI were investigated by transcriptomic and proteomic analysis. By combining gene expression data and weighted gene coexpression network analysis (WGCNA), key target genes related to MI were selected and four key hub genes (MAP3K8, PDE4B, BCL2A1 and FGR) were identified by LASSO, support vector machine (SVM) and Boruta algorithm. These genes were significantly upregulated in patients with MI and showed high diagnostic efficacy. EDCs may enhance the inflammatory response of MI by promoting the infiltration of pro-inflammatory immune cells and inhibiting the function of anti-inflammatory cells. The four key hub genes interacted significantly with many apoptosis regulation proteins. Molecular dynamics simulations and DFT further validated the stable binding of EDCs to target proteins and their potential effects on cardiomyocyte function. This study provides a new insight into the molecular mechanism of EDCs in MI, and provides a theoretical basis for the prevention of cardiovascular diseases and environmental toxicology research.
https://doi.org/10.1016/j.enceco.2025.08.009

Machine learning and SHAP-based identification of RNASE1 linking environmental endocrine-disrupting chemicals exposure to atherosclerosis,
Zhou, X., Xiao, Q. L., Guo, X., Wang, W. N. and Huang, M. D., *Medicine*, Sep 12 2025, Vol. 104, no. 37.

Environmental endocrine-disrupting chemicals (EDCs) are ubiquitous pollutants implicated in cardiometabolic disorders, yet their mechanistic contribution to atherosclerosis (AS) remains elusive. Seven prevalent EDCs - bisphenol A, dibutyl phthalate, di(2-ethylhexyl) phthalate, dioxins, polychlorinated biphenyls (PCBs), perfluorooctanoic acid and PFOS - were selected. Network toxicology integrated ChEMBL, STITCH and SwissTargetPrediction to compile human EDCs targets. Differentially expressed genes were derived from 3 Gene Expression Omnibus AS datasets after batch correction. Key genes were filtered by least absolute shrinkage and selection operator regression and support vector machine-recursive feature elimination (SVM-RFE) and intersected with EDCs targets. Diagnostic performance was evaluated by receiver operating characteristic analysis; functional relevance was assessed by KEGG-GSEA, and feature importance was quantified with SHapley Additive exPlanations (SHAP). A total of 1294 nonredundant EDCs target genes were enriched in lipid and AS and endocrine resistance pathways (FDR < 0.05). From 789 AS differentially expressed genes, least absolute shrinkage and selection operator and SVM-RFE converged on 11 robust candidates. Intersection with EDCs targets pinpointed NTRK3 and RNASE1. Receiver operating characteristic analysis yielded AUCs of 0.777 and 0.859, respectively, with a combined AUC of 0.871. GSEA indicated enrichment of cytokine/chemokine and NOD-like receptor signaling for both genes. SHAP scores highlighted RNASE1 as the dominant predictor (mean SHAP = 0.215), whereas NTRK3 contributed modestly (mean SHAP = 0.005). RNASE1 and NTRK3 were identified as key molecular links between endocrine-disrupting chemical exposure and AS. Among them, RNASE1 was revealed as a novel and dominant predictor, highlighting its unique mechanistic role and potential clinical utility in environmental cardiovascular risk stratification and targeted prevention.
https://doi.org/10.1097/md.0000000000044567

Evaluation de l'exposition

Occitanie : La Lettre de l'Air #32 Pesticides, perturbateurs endocriniens et PFAS (polluants éternels) dans l'air : les résultats d'une première étude inédite en France, 2025 | ATMO Occitanie.

A l'occasion de la Journée Nationale de la Qualité de l'Air, Atmo Occitanie dévoile les résultats du suivi des pesticides dans l'air sur 10 sites d'Occitanie dont les 2 métropoles régionales. https://atmo-occitanie.org/occitanie-la-lettre-de-lair-32-pesticides-perturbateurs-endocriniens-et-pfas-polluants-eternels

Comment se protéger des perturbateurs endocriniens ? 600 étudiants vont mesurer leur exposition aux polluants pendant un an,
France 3 Centre-Val de Loire, 2025/10/27/ 2025.

L'université de Tours cherche 600 étudiants du Centre-Val de Loire, pour mener une expérience scientifique sur un an. Les volontaires seront sensibilisés à leur exposition aux perturbateurs endocriniens, et tenteront de s'en... https://france3-regions.franceinfo.fr/centre-val-de-loire/indre-loire/tours/comment-se-proteger-des-perturbateurs-endocriniens-600-etudiants-vont-mesurer-leur-exposition-aux-polluants-pendant-un-an-3239959.html

Perturbateurs endocriniens: un nouvel outil pour évaluer l'exposition des couples infertiles,
Réalités en Gynécologie-Obstétrique, 2025/09// 2025, no. 228.

Les effets délétères des perturbateurs endocriniens (PE) sur la santé en général et sur la santé reproductive en particulier, ont des niveaux de preuve de plus en plus pertinents. Ces effets peuvent être réversibles en dehors de l'exposition pendant la grossesse mais deviennent irréversibles pendant la grossesse en modifiant l'expression des gènes du fœtus exposé. Le but de cet article est d'identifier les expositions des couples infertiles et d'améliorer leur information pour prévenir les effets des polluants sur leur fertilité et sur la descendance à l'aide d'un questionnaire disponible pour tous les couples consultants en PMA depuis octobre 2021. Au total, 3875 réponses ont été collectées. Ce questionnaire est simple, rapide, pédagogique pour développer l'intérêt des patients à prévenir leurs expositions aux polluants. Cette étude montre des différences de connaissance sur l'exposition aux polluants de l'environnement entre patients infertiles et témoins, mais aussi au sein de la population infertile. https://fertilyon.com/wp-content/uploads/2025/11/Perturbateurs-endocriniens_oct-2025.pdf

Early-Life Dietary Exposure to Perfluorooctanoic Acid (PFOA) Through Milk Consumption: A Systematic Review,
Ahmadpourmir, H., Taghizadeh, S., Tsarouhas, K., Rakhshani, F., Ebrahimi, V., Tsatsakis, A., Tsitsimpikou, C., Hashemzaei, M. and Rezaee, R., *Journal of Applied Toxicology*, 2025.

Perfluorooctanoic acid (PFOA) has raised public concern due to its widespread presence/use and toxic health effects including hepatotoxicity, neurotoxicity, and developmental toxicity. Because dietary intake is a major route of PFOA exposure, and milk is a primary source of nutrition in early life, the present systematic review discusses PFOA occurrence in milk samples and the employed determination methods. In the present article, 69 studies (published 2007-2024) reporting PFOA levels in infant formula, commercial milk, and human breast milk were included. The highest concentration of PFOA in infant formula and commercial milk was reported from Spain (2490 ng/kg)

and the highest level of PFOA in breast milk from Belgium (3.5 ng/mL). The most commonly used approaches for extraction and analysis of PFOA were solid-phase extraction and LC-MS/MS, respectively. The evidence indicates the need for constant monitoring of PFOA levels in milk samples to safeguard vulnerable populations, especially neonates, infants, and children.
https://doi.org/10.1002/jat.4932

Dioxin and PCB monitoring in Greek food products during the period 2002-2022 and preliminary assessment of general population exposure through the diet,
Costopoulou, D., Vassiliadou, I., Kedikoglou, K., Grigoriou, C. and Leondiadis, L., *Food and Chemical Toxicology*, Dec 2025, Vol. 206.

Human dietary exposure to polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), dioxin-like polychlorinated biphenyls (DL-PCBs) and non dioxin-like polychlorinated biphenyls (NDL-PCBs) is of worldwide scientific concern due to the health hazards associated with these compounds. In this study an estimation of the dietary intake of adolescents and adults in Greece was attempted for the first time. Representative samples from food categories widely consumed in Greece were collected and analyzed during a period of 21 years (2002-2022). Occurrence data found were combined with food consumption data available in the EFSA Comprehensive Food Consumption Database, to assess the dietary exposure of the Greek population. The food group with the highest total (PCDD/Fs and DL-PCBs) mean upperbound concentration was "fish and seafood" with 0.71 pg WHO-TEQ g- 1 wet weight (ww) (9.68 pg WHO-TEQ g- 1 fat) and the one with the lowest mean WHO-TEQ concentration was the "vegetable oil" group, 0.35 pg WHO-TEQ g- 1 fat. The highest amounts of indicator PCBs (ind-PCBs), were detected in the "fish and seafood" category (5.25 ng g- 1 ww, 86.8 ng g- 1 fat) whereas the lowest mean concentration was found in eggs (1.56 ng g- 1 fat). For adult Greek population the average daily intake in PCDD/Fs and DL-PCBs is 1.02 pg WHO-TEQ kg body weight- 1 (bw), which corresponds to 7.14 pg WHO-TEQ kg bw- 1 weekly intake whereas the average daily intake in ind.-PCBs is 5.51 ng kg bw-1. The main contributor to the total dietary intake in PCDD/Fs and PCBs is the "fish and seafood" category. The general background dietary exposure of the Greek population to PCDD/Fs and DL-PCBs estimated is within the tolerable daily intake (TDI) value range of 1-4 pg WHO-TEQ kg bw -1 proposed by the WHO in 1998, but exceeds the tolerable weekly intake (TWI) of 2 pg WHO-TEQ kg bw- 1 proposed in the updated scientific opinion of the EFSA CONTAM Panel in 2018.
https://doi.org/10.1016/j.fct.2025.115717

Assessment of chemical extracts of urban air for endocrine disruption using a serie of in vitro bioassays: a case study in Montreal, Canada,
Gillet, A. P., Dong, H., Liu, L., Akiki, C., Zhang, X., Tian, L., Wania, F., Wade, M. G., Apparicio, P., Bayen, S. and Delbes, G., *Chemosphere*, 2025/11/15/ 2025, Vol. 393, p. 144760.

Recent data indicate that urban air harbors a complex mixture of industrial chemicals, pesticides, and combustion by-products, many of which may act as endocrine-disrupting chemicals (EDCs). By interfering with the endocrine system, EDCs can affect human health. Hence, there is an urgent need to better characterize outdoor airborne chemical mixtures and their health impact. This study assessed the bioactivity on key targets of EDCs for chemical extracts of the atmospheric vapour phase (i.e., excluding particulate matter) collected from 40 sites across Montreal, Canada, using passive air samplers deployed over 82 summer days. Seven validated bioassays were used to test the ability of each extract to alter the estrogen, androgen, thyroid, and steroidogenesis pathways. Of the 42 urban air extracts tested, none induced alteration of the human thyroid peroxidase activity or activated the human androgen receptor (hAR) but three induced estrogen receptor activation and five inhibited the sodium/iodide symporter by 40-60 %. More than 20 extracts

antagonized hESR1 and/or hAR, a few with very strong potency. Yet, blanks used as controls also induced signals in the antagonist mode of the transactivation assays and affected testosterone production in the H295R steroidogenic assay, challenging data interpretations. Overall, our data indicate the potential for thyroid, estrogenic, antiestrogenic and antiandrogenic disruption caused by the chemical mixtures present in the outdoor air of a major metropolis. This work provides one of the first integrated assessments of endocrine activity from atmospheric vapour phase chemical extracts, underscoring the importance of incorporating bioanalytical tools into air-quality and health-risk evaluation frameworks. https://doi.org/10.1016/j.chemosphere.2025.144760

Per-and polyfluoroalkyl substances (PFAS) in milk and dairy products: a literature review of the occurrence, contamination sources, and health risks,
Hossini, H., Massahi, T., Parnoon, K. and Nouri, M., *Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment*, Sep 2 2025, Vol. 42, no. 9, p. 1284-1296.

Per-and polyfluoroalkyl substances (PFAS) are man-made chemicals valued for their unique characteristics, such as their ability to withstand heat, water, and oil. These compounds are widely utilized across a range of applications. Therefore, the existence of these compounds in the environment and their accumulation in various ecosystems is a cause for concern regarding their potential health risks. Considering the importance of dairy products in the human diet, this review examines the global occurrence, sources, and health risks of PFAS contamination in milk and dairy products (hereinafter referred to as "MDPs"). The results of the PFAS detection in the reviewed studies show a diverse contamination pattern influenced by local industrial activities, agricultural practices and regulatory measures. PFAS have been detected in various MDPs, with significant contamination near industrial areas. MDPs are indicated to be significant vectors of individual exposure to PFAS, with contamination arising primarily from dairy animal feed, water and atmospheric sediments, as well as food processing materials. The health effects of PFAS exposure through MDPs consumption, particularly the risk of endocrine disruption, immunosuppression, and carcinogenicity, are also discussed. This review highlights the need for global standards and policy measures, encompassing stricter regulations on industrial emissions, agricultural practices, and more, to effectively reduce PFAS contamination in MDPs and safeguard consumer health.
https://doi.org/10.1080/19440049.2025.2538224

Evaluation of EDCs (phthalates, bisphenols, parabens, and benzophenones) in coffee: cross-sectional study in Algiers,
Khelfi, A. and Azzouz, M., *Food Chemistry*, Dec 15 2025, Vol. 495.

*Endocrine disrupting themicals (EDCs) are emerging environmental pollutants. The present study focused on evaluating the concentrations of EDCs in packed coffee.
 Among 12 investigated EDCs, only DEP, DEHP, DnBP, BPA, and BPF were found in packed coffee (20 96, 40 56, 80 96, 20 96, and 20 9%, respectively). The mean values ranged from 0.230 ng/g for BPA to 23.214 ng/g for DnBP. DnBP was the most frequently detected EDC in coffee powder (60%), followed by DEP, DEHP, BPA, and BPF (20 9% each).
 Migration assessment showed that DEHP, DnBP, and BPF amounts were significantly higher after coffee preparation in the traditional coffee maker (2.515 vs 2.192 ng/ml, 1.845 vs 1.491 ng/ml, and 0.177 vs <LD ng/mL).
 The levels of phthalates and BPA did not exceed the specific migration limits (SMEs) and the estimated daily intake (EDI) to EDC were low. Hazard quotients (HQs) were below 1.0 for general and highly exposed populations.*
https://doi.org/10.1016/j.foodchem.2025.146465

From screening to risk assessment: a comparative study on product usage, human burden, and potential neurotoxicity of novel paraben analogues,
Meng, L. X., Kuang, H. X., Tan, J. H., Li, X. L., Liu, Y., Xiang, M. D., Zhou, Y., Fan, R. F. and Yu, Y. J., *Environment International*, Oct 2025, Vol. 204.

Parabens are extensively used preservatives with endocrine disrupting effects and neurotoxicity. Their restricted usage may drive the development of alternatives for producing preservative-free products. Nevertheless, the prevalence and health risks of paraben analogues remain poorly understood. Herein, we screened potential paraben analogues using high-resolution mass spectrometry and assessed their prevalence in personal care products (PCPs) and population exposure trends. We first identified p-hydroxyacetophenone (PhAc), a structural analogue of parabens, in children's urine based on the common fragmentation characteristics of parabens. Quantitative analysis revealed that the average content of PhAc in PCPs was 2-38 times higher than that of typical parabens. Furthermore, the longitudinal biomonitoring study conducted from 2016 to 2023 revealed that the geometric mean levels of PhAc in the urine of children aged 5-13 years in South China increase from 35.20 mu g/L to 102.68 mu g/L, which is 1-3 orders of magnitude greater than parabens. Nevertheless, PhAc is not a permitted preservative in PCPs and its health risk is unclear. To investigate the potential neurotoxicity of extensively present PhAc, neuronal cells were exposed to different concentrations of PhAc and typical parabens for 24 h, respectively. The results indicated that PhAc exhibited greater potential neurotoxicity than methylparaben, the most widely used paraben. Even exposure to doses comparable to urinary PhAc concentrations (100 nM-1 mu M) could significantly disrupt metabolism homeostasis, damage cell membranes and morphology, and increase apoptosis rate in neuronal cells. Therefore, PhAc, a new paraben analogue with wider product applications, higher human exposure, and greater potential neurotoxicity, may pose considerable ecological and human health risks. https://doi.org/10.1016/j.envint.2025.109805

Predicting Dermal Exposure to Semivolatile Organic Compounds Resulting from Direct Contact with Consumer Products,
Song, Z. D., Nian, L. Y., Wu, Y. L., Fan, Y. J., Ren, X. P., Zhang, W. J. and Xu, Y., *Environmental Science & Technology*, Oct 28 2025, Vol. 59, no. 42, p. 22713-22726.

Dermal exposure through direct contact with consumer products is an important yet often overlooked pathway for human exposure to semivolatile organic compounds (SVOCs). In this study, a single-layer transient model was developed to improve our understanding of dermal exposure to SVOCs under direct contact scenarios. Using human skin equivalents combined with a Franz-type diffusion cell, an innovative experimental system was implemented to determine key model parameters, specifically skin diffusion and partitioning parameters (D epi and K epi/source), for 16 SVOCs across seven types of consumer products. The results demonstrate that using traditional permeability coefficients without considering the contact source can lead to inaccuracies in dermal exposure assessments. The model and measured parameters were validated against data from human subject studies, showing good agreement. Additionally, correlations between the key model parameters and the physicochemical properties of SVOCs were identified. Dermal exposure doses and associated health risks under various direct contact scenarios were assessed, with many cases showing hazard quotients near or above 1 and cancer risks exceeding 10-4, highlighting its importance as a significant exposure pathway for SVOCs. This study provides valuable experimental and modeling tools for prioritizing SVOCs and guiding regulatory decisions on limiting their use in consumer products, thereby reducing potential health risks from dermal exposure.
https://doi.org/10.1021/acs.est.5c06786

Integrated chemical exposome-metabolome profiling of follicular fluid and associations with fertility outcomes during assisted reproduction,
Young, A. S., Gennings, C., Braselton, M. E., Mullins, C. E., Jariwala, P., Liang, D. H., Spencer, J. B., Smith, A. K., Hipp, H., Shang, W. R., Abhari, S., Knight, A. K., Gaskins, A. J. and Walker, D. I., *Environment International*, Sep 2025, Vol. 203.

Many endocrine-disrupting chemicals have been linked to impaired ovarian function and fertility. However, most research has focused on small numbers of known chemicals in blood or urine. We aimed to measure the untargeted chemical exposome and metabolome in follicular fluid, a more toxicologically relevant reproductive biofluid, and evaluate associations with outcomes of controlled ovarian stimulation. Follicular fluid was collected from 82 patients undergoing egg retrieval for assisted reproduction in Atlanta and analyzed using untargeted gas (GC) and liquid (LC) chromatography with high-resolution mass spectrometry (HRMS). In single-chemical regression and mixture models (weighted quantile sum with random subsets), we estimated associations of chemicals with retrieved oocyte count, adjusted for age, race, smoking, and ovarian stimulation protocol. In over 90% of follicular fluid samples, we detected 82 confirmed exogenous chemicals with known identities as plasticizers, flame retardants, pesticides, per- and polyfluoroalkyl substances, or polycyclic aromatic hydrocarbons. About 3,081 of the untargeted detected features were individually associated with fewer retrieved oocytes after multiple-testing correction. In the GC environmental mixture model, 587 untargeted chemical features were jointly associated with 21% fewer retrieved oocytes (95% CI: -30 %, -12 %) per standard-deviation (SD) increase in exposure, compared to average single-chemical effects of -10 % per SD. Twenty metabolic pathways were associated with chemical mixture indices and oocyte count, including methionine, nicotinamide, glycine, pyrimidine, selenocompounds, tryptophan, phenylacetate, and biopterin metabolism. Our findings suggest that complex chemical mixtures infiltrate oocyte microenvironments and may impair ovarian reserve through diverse mechanisms. Discovery-based untargeted exposomic approaches uncover new exposures of potential concern and highlight the larger effects of cumulative mixtures than any single chemical alone. https://doi.org/10.1016/j.envint.2025.109787

Méthodes

Advancement of electrochemical sensors in the detection of estrogen steroids in the environment: A critical review,
Farale, H., George, M. and Kanchi, S., *Journal of Environmental Chemical Engineering*, Oct 2025, Vol. 13, no. 5.

Estrogenic steroids, both natural and synthetic, are found in the environment and pose a significant risk to humanity and nature at even very low levels. Electrochemical sensors are an exciting option to replace traditional analytical methods due to their high sensitivity, portability, and real-time monitoring potential. This study aims to provide a critical review of recent improvements in electrode platforms, including glassy carbon, indium tin oxide, gold, screen-printed electrodes, and paper-based electrodes, enhanced with nanomaterials, i.e., graphene, quantum dots, molecularly imprinted polymers, and aptamers. Femtomolar limits of detection have been achieved, with the value of 0.5 x 10-15 M L-1 for a graphene oxide-modified aptasensor. These platforms have performed well in analysis in complex matrices, including wastewater, milk, serum, and river water. Progress has been made, but concerns and challenges regarding the stability, reproducibility, and performance of electrochemical sensors in complex environmental matrices still exist. Future opportunities for the use of electrochemical sensors to combat environmental risk assessment of

estrogenic steroids lie in miniaturized and multiplex devices with integrated AI/ML algorithms to interpret the signal and create a platform for macro environmental monitoring. Without a doubt, electrochemical sensors provide great potential for sustainable management of water quality and environmental risk assessment. https://doi.org/10.1016/j.jece.2025.119094

A deep-learning approach to predict reproductive toxicity of chemicals using communicative message passing neural network,
He, O. W., Chen, D. X. and Li, Y. M., *Frontiers in Toxicology*, Jul 22 2025, Vol. 7.

Reproductive toxicity is a concern critical to human health and chemical safety assessment. Recently, the U.S. Food and Drug Administration announced plans to assess toxicity with artificial intelligence-based computational models instead of animal studies in "a win-win for public health and ethics." In this study, we used a reproductive toxicity dataset using Simplified Molecular Input Line Entry Specifications (SMILES) to represent 1091 reproductively toxic and 1063 non-toxic small-molecule compounds. A repeated nested cross-validation procedure was applied, in which the dataset was randomly partitioned into five distinct folds in the outer loop, each time, one fold serving as the test set. In the inner loop, a similar procedure was also repeated five times, with 12.5% each time serving as the validation set. We first evaluated the performance of classical machine learning (ML) methods such as Random Forest and Extreme Gradient Boosting on predicting reproductive toxicity, using standard model evaluation metrics including accuracy score (ACC), the area under the curve (AUC) of the receiver operating characteristics curve (ROC) and F1 score. Our analyses indicate that these methods' overall results were mediocre and insufficient for high-throughput screening. To overcome these limitations, we adopted the Communicative Message Passing Neural Network (CMPNN) framework, which incorporates a communicative kernel and a message booster module. Our results show that our ReproTox-CMPNN model outperforms the current best baselines in both embedding quality and predictive accuracy. In independent test sets, ReproTox-CMPNN achieved a mean AUC of 0.946, ACC of 0.857 and F1 score of 0.846, surpassing traditional algorithms to establish itself as a new state-of-the-art model in this field. These findings demonstrate that CMPNN's deep capture of multi-level molecular relationships offers an efficient and reliable computational tool for rapid chemical safety screening and risk assessment. https://doi.org/10.3389/ftox.2025.1640612

Application of the AI-Based Framework for Analyzing the Dynamics of Persistent Organic Pollutants (POPs) in Human Breast Milk,
Jovanovic, G., Bezdan, T., Romanic, S. H., Saric, M. M., Biosic, M., Mendas, G., Stojic, A. and Perisic, M., *Toxics*, Jul 27 2025, Vol. 13, no. 8.

Human milk has been used for over 70 years to monitor pollutants such as polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs). Despite the growing body of data, our understanding of the pollutant exposome, particularly co-exposure patterns and their interactions, remains limited. Artificial intelligence (AI) offers considerable potential to enhance biomonitoring efforts through advanced data modelling, yet its application to pollutant dynamics in complex biological matrices such as human milk remains underutilized. This study applied an AI-based framework, integrating machine learning, metaheuristic hyperparameter optimization, explainable AI, and postprocessing, to analyze PCB-170 levels in breast milk samples from 186 mothers in Zadar, Croatia. Among 24 analyzed POPs, the most influential predictors of PCB-170 concentrations were hexa- and hepta-chlorinated PCBs (PCB-180, -153, and -138), alongside p,p'-DDE. Maternal age and other POPs exhibited negligible global influence. SHAP-based interaction analysis revealed pronounced co-behavior among highly chlorinated congeners, especially PCB-138-PCB-153, PCB-138-PCB-180, and PCB-180-PCB-153. These findings highlight the importance of examining pollutant interactions

rather than individual contributions alone. They also advocate for the revision of current monitoring strategies to prioritize multi-pollutant assessment and focus on toxicologically relevant PCB groups, improving risk evaluation in real-world exposure scenarios. https://doi.org/10.3390/toxics13080631

Assessment of Endocrine-Disrupting Properties in Cosmetic Ingredients: Focus on UV Filters and Alternative Testing Methods,
Maddaleno, A. S., Guardia-Escote, L., Vinardell, M. P., Teixidó, E. and Mitjans, M., *Cosmetics*, Aug 16 2025, Vol. 12, no. 4.

Endocrine-disrupting chemicals are substances capable of interfering with hormonal systems, potentially leading to adverse developmental, reproductive, neurological, and immune effects in both humans and wildlife. Various experimental models are currently available to assess the endocrine-disrupting potential of substances. However, in the context of cosmetic ingredients, the ban on animal testing for safety and efficacy evaluations in Europe and other regions necessitates the use of in vitro or in silico approaches. Concerns have been raised regarding the possible endocrine-disrupting properties of certain cosmetic compounds, prompting the development of a priority substance list that includes several ultraviolet (UV) filters. This review provides a comprehensive overview of the main methodologies employed to evaluate endocrine-disrupting effects, with a particular focus on different endocrine organs. It also compiles and analyzes literature data related to commonly used UV filters such as benzophenones, avobenzone, homosalate, octocrylene, octinoxate, and 4-methylbenzylidene camphor. A major limitation identified is the lack of validated in vitro methods for assessing disruptions in specific endocrine organs, such as the thyroid and pancreas. This gap hinders accurate interpretation of experimental results and highlights the urgent need for further research to clarify the safety profiles of UV filters and other cosmetic ingredients. https://doi.org/10.3390/cosmetics12040175

Electrochemical Determination of Bisphenol a Using a Drop-Dry Modified Gold Electrode with Metal-Organic Framework, Quantum Dots, and their Composite,
Oloyede, S. O. and Ajibade, P. A., *Chemistryopen*, 2025.

A modified gold electrode with metal-organic frameworks (MOFs), quantum dots (QTs) and their composite are fabricated to determine bisphenol A. The chemically modified sensors are characterized using ultraviolet-visible, Fourier transform infrared spectroscopy spectra, X-ray diffraction, scanning electron microscopy, and ransmission electron microscopy. Upon examining the electrochemical characteristics of the fabricated sensors, it is discovered that the QDs@MOFs conjugate performs better than the metal-organic frameworks and quantum dots, which could be attributed to the better conductivity of the conjugate. The effects of pH, accumulation time, and sensor concentration are studied at optimal condition. Over a wide range of bisphenol A (BPA) concentrations (1 mu M-14 mu M), the limit of detection is found to be 0.470 mu M and the limit of quantitation is 1.425 mu M. The results indicate that the electrochemical sensor fabricated from composite modified gold electrode is efficient for the detection of bisphenol A. The stability and reproducibility of the sensor are also evaluated. https://doi.org/10.1002/open.202500327

Tailoring flexible aliphatic covalent organic frameworks with hydroxyl sites: A novel platform for efficient extraction and rapid detection of bisphenols,
Su, L., Wang, L., Zhao, L., Liu, Y., Wang, C., Shao, C., Liu, L., Zhang, D. and Darwish, I. A., *Talanta*, 2025/11/15/ 2025, Vol. 299, p. 129134.

The development of advanced adsorbents enabling rapid and sensitive detection of endocrine-disrupting bisphenols (BPs) is essential for safeguarding ecosystems and human health. Covalent

organic frameworks (COFs) hold great promise for the adsorption of BPs, but conventional rigid aromatic architectures suffer from limited molecular recognition capability. Herein, we design a hydroxyl-functionalized flexible aliphatic COF (TFT-TAH COF) via the polymerization of 2,3-dihydroxydicarbohydrazid (TAH) and 1,3,5-tris(4-formyl-phenyl) triazine (TFT) for efficient extraction and sensitive detection of BPs (BPA, BPF, BPAF, and BPF). The flexible aliphatic linker exposes more active sites, thereby displaying excellent BPs adsorption capacity (654-1111 mg g-1) and rapid adsorption kinetics (equilibrium within 30 s). TFT-TAH COF gave good affinity for BPs through the synergistic effects of size matching, hydrogen bonding, and π-π interactions. In addition, a novel analytical method was developed for BPs determination by coupling TFT-TAH COF-based dispersive solid-phase extraction with high-performance liquid chromatography, achieving low detection limits of 0.03-0.1 ng mL-1 and satisfactory precision with relative standard deviations≤5.7 %. Moreover, recoveries for the spiked lake, river, drinking water, bottled water, and milk samples ranged from 89.8 to 101.6 %. This work pioneers an innovative approach to fabricating flexible aliphatic-linked COFs for environmental monitoring and food safety. https://doi.org/10.1016/j.talanta.2025.129134

Machine learning-driven prediction models and mechanistic insights into cardiovascular diseases: deciphering the environmental endocrine disruptors nexus,
Yu, W.-M., Chen, Y.-P., Cheng, A.-L., Zheng, Z.-Y., Wang, J.-W., Liu, X.-B. and Zhou, J.-X., *Journal of Translational Medicine*, 2025/11/12/ 2025, Vol. 23, no. 1, p. 1272.

BACKGROUND: Cardiovascular disease (CVD) persists as the foremost cause of global mortality, yet the mechanistic links between environmental pollutants and CVD pathogenesis remain poorly defined. This study addresses this gap by integrating machine learning-driven epidemiology with computational biology to systematically evaluate the role of endocrine-disrupting chemicals (EDCs) in CVD development. METHOD: We analyzed data from the NHANES cohort to identify CVD-associated EDCs using advanced predictive modeling. Molecular docking and dynamics simulations were employed to characterize interactions between prioritized compounds and the NOX2-p22phox complex, a key regulator of oxidative stress. Structural and functional impacts on NADPH oxidase activity were assessed through residue-level binding analysis and reactive oxygen species (ROS) quantification. RESULTS: Machine learning identified 3-hydroxyfluorene (3-HF) as a novel environmental risk factor for CVD. Molecular simulations revealed that 3-HF selectively binds to the transmembrane domain of the NOX2-p22phox complex, forming stable interactions with residues critical for structural integrity (e.g. T135, H160). These interactions destabilized the protein complex, impairing NADPH oxidase assembly and suppressing ROS generation. Further analysis demonstrated that 3-HF-mediated oxidative stress disruption correlates with vascular dysfunction pathways implicated in CVD progression. CONCLUSION: This study establishes 3-HF as a redox-disrupting environmental contaminant contributing to CVD through NOX2-p22phox targeting. By bridging population-level exposure data with atomic-scale mechanistic insights, our work provides a transformative framework for environmental health risk assessment and preventive intervention design. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s12967-025-07223-6. https://doi.org/10.1186/s12967-025-07223-6

Non-Targeted Analysis Workflow of Endocrine-Disrupting Chemicals in Ovarian Follicular Fluid: Identification of Parabens by Diagnostic Fragmentation Evidence and Additional Contaminants via Mass Spectral Library Matching,
Zhou, Z. L., Neal, M. S., Foster, W. G. and Feng, Y. L., *Acs Measurement Science Au*, 2025.

Ubiquitously distributed in the environment, food supply, and consumer products, endocrine-disrupting chemicals (EDCs) are exogenous substances that disrupt hormonal activities in the endocrine system. Increasing evidence suggests that women with reproductive disorders tend to

accumulate higher levels of EDCs, such as phthalates and parabens, in ovarian follicular fluid. However, most existing studies focus on the measurements of a limited number of prevalent EDCs, overlooking chemicals and metabolites that are not known or prioritized. To address the knowledge gap, we developed a non-targeted analysis (NTA) workflow for broader EDC detection in follicular fluid samples using liquid chromatography-high-resolution mass spectrometry (LC-HRMS). By taking advantage of the higher-energy collisional dissociation (HCD) in the Orbitrap mass spectrometer, we first identified up to 17 characteristic product ions for parabens and their metabolites. Compared to conventional mass spectral matching via online databases and in silico fragmentation algorithms, paraben precursor ion prioritization through such diagnostic fragment ion extraction achieved more accurate compound identification at concentrations as low as 1 ng/mL. To extend the chemical coverage beyond known fragmentation patterns, we also assessed mass spectral library search via Compound Discoverer software, along with retention time model predictions. As a proof-of-concept application, the entire workflow was applied to a pooled follicular fluid sample collected from 211 Canadian patients receiving fertility treatment. Our compound identification results revealed that parabens could undergo several possible metabolic pathways, including hydrolysis, hydroxylation, sulfation, and amino acid conjugation. Furthermore, a total of 14 compounds were identified with level 1 confidence, including EDCs and their metabolites such as monophthalates, UV filters, and phenolic acids. The underlying implications of reproductive health associated with these substances are an area for future study. https://doi.org/10.1021/acsmeasuresciau.5c00082

Bioinformatics analysis to identify endocrine-disrupting chemicals targeting key ESCC-related genes,
Zhu, Y. N., Shen, W. T. and Li, M. Y., *Toxicology Mechanisms and Methods*, 2025.

Esophageal squamous cell carcinoma (ESCC), which has a high incidence and mortality rate in East Asia, arises from a complex interplay between genetic alterations and environmental exposures. Among environmental risk factors, endocrine-disrupting chemicals (EDCs) have attracted widespread attention, yet their impact on ESCC via gene interactions remains underexplored. This study integrated bioinformatics analysis to identify key genes and EDCs associated with ESCC pathogenesis. Chemical-gene interaction data were obtained from the Comparative Toxicogenomics Database(CTD), and differentially expressed genes(DEGs) were screened from the Gene Expression Omnibus (GEO) database. LASSO regression analysis prioritized five key genes (BUB1B, TPM2, KRT17, ADH1B, SALL4). Based on these genes, 25 EDCs potentially involved in ESCC were identified, of which 13 (such as benzo[a]pyrene) targeted at least three of the key genes. These findings suggested a novel EDC-gene-ESCC interaction network and provide insights into the environmental mechanisms underlying ESCC, offering potential targets for risk assessment and therapeutic intervention. https://doi.org/10.1080/15376516.2025.2543347

Documents INRS

Perturbateurs endocriniens,
Travail et sécurité, INRS, n°873, p.50, septembre 2025
Réponse d'un expert INRS à la question suivante : en entreprise, comment prévenir les risques liés aux perturbateurs endocriniens ?
https://www.travail-et-securite.fr/ts/pages-transverses/liseusePDF.html?pdfUuid=jcr:b3a3cb44-6b3e-4a38-a0d5-36649a62ca20

Les perturbateurs endocriniens,
Dépliant INRS, ED 6377, 2ème édition, 2025
Ce dépliant fait le point sur les risques liés aux perturbateurs endocriniens en milieu de travail. Après avoir rappelé la définition d'un perturbateur endocrinien, il répertorie les sources d'exposition et les effets potentiels sur la santé, et rappelle les règles générales de prévention.
https://www.inrs.fr/media.html?refINRS=ED%206377

Replay du webinaire : Perturbateurs endocriniens : les repérer pour prévenir les risques en entreprise – INRS, novembre 2025
Comment repérer et inventorier les perturbateurs endocriniens et les produits qui en contiennent en milieu professionnel ? Quels outils utiliser ? Quelles sont les sources et les situations d'exposition ? Quelles sont les grandes lignes de la démarche prévention ? Ce webinaire est destiné à tous ceux qui souhaitent identifier et repérer les perturbateurs endocriniens dans leur entreprise, et mettre en place des mesures de prévention adaptées. https://www.inrs.fr/media.html?refINRS=Anim-498

Perturbateurs endocriniens : un nouvel outil pour les repérer en milieu de travail
GHEZZI-TOURNADE F. ; RICAUD M. *Références en santé au travail*, n°183, pages 5-6, septembre 2025, INRS.
L'INRS met à disposition un nouvel outil de repérage des perturbateurs endocriniens et actualise son dossier web sur le sujet https://www.inrs.fr/media.html?refINRS=AC%20196

Repérage des perturbateurs endocriniens en entreprise - Outil - INRS.
avril 2025
Cet outil d'aide au repérage des perturbateurs endocriniens en milieu de travail rassemble 344 substances chimiques, produites en grande quantité et classées pour leurs effets avérés ou potentiels de perturbation endocrinienne (par l'Anses et/ou par le site institutionnel EDLists). Pour chaque substance, les principaux secteurs industriels et usages (passés et actuels) concernés sont recensés. Sont également renseignés pour chaque substance, le numéro CAS, la catégorie au regard des effets de perturbation endocrinienne sur la santé, et le cas échéant, la classification CMR (règlement européen CLP), le ou les tableaux de maladies professionnelles ainsi que la fiche toxicologique associés. https://www.inrs.fr/media.html?refINRS=outil16

Evaluation du danger des substances chimiques : des différences selon le sexe mieux comprises, mais des lacunes à combler
SPONNE I. ; DARNE C. ; VALENTINO S. *Hygiène et sécurité du travail*, n°280, p. 49-56, septembre 2025, INRS
En avril 2022, chez l'humain, on comptait 19 969 gènes codant pour des protéines. Que l'on soit homme ou femme, 99 % de ces gènes sont identiques. Pour autant, le capital chromosomique sexuel des hommes et des femmes est à l'origine de sensibilités différentes vis-à-vis de l'environnement. Le sexe est donc une variable essentielle à intégrer au moment de l'évaluation d'un danger et de la caractérisation de la toxicité des substances chimiques rencontrées en milieu professionnel ; cette toxicité peut aussi affecter la descendance de la personne exposée. Cet article met en relief les connaissances acquises sur les différences de toxicité liées au sexe et celles restant à développer pour mieux évaluer le danger des substances chimiques et les risques professionnels auxquels les travailleuses et travailleurs sont exposés. https://www.inrs.fr/media.html?refINRS=DO%2049-5

Agenda, politique, actualité, société et évaluation du caractère PE des substances

2026 Environmental Endocrine Disruptors Conference GRC.
The 2026 GRC on Environmental Endocrine Disruptors will be framed around four cutting-edge multidisciplinary topics: 1) the identification of new EEDs and disease pathways altered by these chemicals; 2) emerging technologies to measure EEDs and model their effects, including the development of New Approach Methodologies (NAMs) and methods to evaluate mixtures; 3) the influence of individual characteristics (like occupation, sex, and age) on exposures and effects of EEDs; and 4) mitigating the effects of EEDs through personalized interventions, policies, and regulations. With its focus on emerging approaches and interventions, discussion will emphasize ways to integrate results from laboratory studies, wildlife studies, and epidemiological studies; using this approach will allow participants to obtain a comprehensive, translational view of how EEDs affect the health of individuals, populations, and ecosystems.
https://www.grc.org/environmental-endocrine-disruptors-conference/2026/

CleanScreen : un nouvel outil pour la substitution des PFAS dans l'industrie électronique, INERIS
ChemFORWARD lance une application destinée à soutenir la formulation de nettoyants et dégraissants plus sûrs pour l'industrie électronique
https://substitution-perfluores.ineris.fr/fr/node/281

Commission restricts the use of 'forever chemicals' in firefighting foams,
European Commission
Today, the Commission adopted new measures restricting the use of PFAS (per- and polyfluoroalkyl substances) in firefighting foams under the REACH Regulation, the EU's chemicals legislation. This is an important measure that protects people and the environment from the risks posed by PFAS.https://ec.europa.eu/commission/presscorner/detail/en/ip_25_2286

Consultation on PFAS draft opinion – Guidance for respondents, ECHA
L'Agence européenne des produits chimiques prévoit de lancer une consultation sur le projet d'avis de son Comité d'analyse socio-économique (SEAC) concernant la restriction proposée à l'échelle de l'UE des substances perfluoroalkylées et polyfluoroalkylées (PFAS) à la suite de la réunion du Comité en mars 2026. La consultation se déroulera au moyen d'un questionnaire structuré, invitant les participants à répondre à des questions sur les impacts potentiels d'une restriction de l'utilisation des PFAS dans différents secteurs. Il leur sera également demandé de fournir des informations précises sur la disponibilité et la faisabilité d'alternatives à ces substances chimiques largement utilisées. Le replay du webinaire qui détaille l'objectif de la consultation, la structure du questionnaire de consultation, le type d'informations est demandé dans l'enquête et comment préparer les données pour la consultation, est disponible
https://echa.europa.eu/-/webinar-consultation-on-pfas-draft-opinion

Highlights from September RAC and SEAC meetings. ECHA
Lors de leurs réunions de septembre, les comités d'évaluation des risques (RAC) et d'analyse socio-économique (SEAC) ont poursuivi l'évaluation de la proposition européenne visant à limiter l'utilisation des substances perfluoroalkylées et polyfluoroalkylées (PFAS) . Le SEAC a formulé des conclusions provisoires concernant l'utilisation des PFAS dans les secteurs de l'énergie et des lubrifiants, tandis que le RAC a formulé des conclusions provisoires concernant l'électronique et les semi-conducteurs. Les deux comités ont entamé des discussions sur la fabrication des PFAS et ont continué d'examiner des questions transversales telles que les seuils de concentration au-delà desquels l'utilisation des PFAS pourrait être restreinte, les évaluations des dangers et les mesures

générales de gestion des risques pour surveiller et réduire les émissions dans l'environnement. Par ailleurs, le SEAC a entamé des discussions sur l'électronique et les semi-conducteurs.
https://echa.europa.eu/-/highlights-from-september-2025-rac-and-seac-meetings

L'Ineris publie un état des lieux sur les usages des PFAS et alternatives documentées, INERIS
Ce rapport dresse un panorama détaillé des usages des PFAS et de leurs alternatives, couvrant de nombreux secteurs et applications. Il peut servir d'outil de référence pour accompagner leur substitution progressive en France et en Europe
https://substitution-perfluores.ineris.fr/fr/actualites/lineris-publie-etat-lieux-usages-pfas-alternatives-documentees

La restriction européenne des PFAS dans les mousses anti-incendie est adoptée, INERIS
Le 2 octobre 2025, la Commission européenne a adopté une restriction sur les substances per- et polyfluoroalkylées (PFAS) dans les mousses anti-incendie
https://substitution-perfluores.ineris.fr/fr/actualites/restriction-europeenne-pfas-dans-mousses-anti-incendie-est-adoptee

Mapping of PFAS uses evaluated in the SEAC draft opinion, ECHA
L'ECHA prévoit de lancer la consultation sur le projet d'avis de son comité d'analyse socio-économique (SEAC) concernant la proposition de restriction des PFAS peu après son accord prévu en mars 2026. La consultation comprendra des questions générales sur tous les différents aspects couverts dans le projet d'avis du SEAC, ainsi que des questions détaillées sur chacune des évaluations sectorielles spécifiques réalisées par le comité. Afin d'aider les parties prenantes à identifier l'évaluation sectorielle à laquelle leur utilisation est soumise, l'ECHA publie cette première cartographie des utilisations des secteurs évalués dans le projet d'avis du SEAC. Une mise à jour de cette cartographie sera publiée après la réunion plénière du SEAC en décembre 2025, lorsque les évaluations sectorielles restantes auront été provisoirement conclues
https://echa.europa.eu/documents/10162/111425157/draft_use_mapping_pfas_en.pdf

Outil d'aide à l'identification des PFAS, INERIS
pfasID est un nouvel outil web dont le but est de faciliter l'identification des PFAS parmi les produits chimiques des chaînes d'approvisionnement. Cette identification s'appuie sur les bases de données de l'OCDE et de l'USEPA et sur des définitions de nomenclature chimique. Pour chaque produit saisi, pfasID fournit différents niveaux d'identification : « Pass » si la substance ne figure pas dans les bases de données et ne contient pas d'alerte structurelle ; « Fail » si la substance est répertoriée dans une des bases ; « Warning » si la structure de la substance indique un statut PFAS potentiel sur la base des définitions de l'ECHA, de l'OCDE, de l'Ontochem et/ou de l'EPA. Cet outil représente le premier volet du projet de PFACTS, visant à créer un centre d'échange de données, d'outils et de connaissances communautaires afin : De simplifier l'identification des produits chimiques et des matériaux PFAS ; D'accélérer la découverte d'alternatives plus sûres aux PFAS à l'aide de l'IA générative ; De recommander des méthodes pour éliminer les PFAS des applications industrielles jusqu'à la mise en place de substituts
https://substitution-perfluores.ineris.fr/fr/actualites/lancement-dun-outil-daide-lidentification-pfas

Replay - Conférence Perturbateurs endocriniens, mythes et réalités / Afis Science - Association française pour l'information scientifique,
Conférence animée par Luc Multigner, Directeur de recherche émérite à l'Institut National de la Santé de de la Recherche Médicale (Inserm), spécialisé dans l'étude des conséquences sanitaires entrainés par les contaminants chimiques de l'environnement

https://www.afis.org/Video-Conference-Perturbateurs-endocriniens-mythes-et-realites

What you need to know about the updated PFAS restriction dossier, KEMI - Agence suédoise des produits chimiques
This summary sets out the main points of the Background Document for the proposed universal PFAS restriction under the REACH Regulation. The Background Document describes the environmental and human health risks associated with the use of PFASs and assesses the appropriateness (proportionality) of different restriction options to address them
https://www.kemi.se/publikationer/rapporter-fran-samarbetsprojekt/2025/what-you-need-to-know-about-the-updated-pfas-restriction-dossier

Perturbateurs endocriniens : le Médipôle Hôpital Mutualiste propose une plateforme ludique et accessible à tous pour sensibiliser le grand public et les professionnels, 2025/11/14
Le Médipôle Hôpital Mutualiste, soutenu par l'ARS Auvergne-Rhône-Alpes, lance une plateforme de jeux en ligne pour sensibiliser le grand public aux perturbateurs endocriniens. Ludique et accessible, elle explique ce qu'ils sont, comment ils se cachent dans notre quotidien et propose des conseils pratiques pour réduire son exposition
https://www.auvergne-rhone-alpes.ars.sante.fr/perturbateurs-endocriniens-le-medipole-hopital-mutualiste-propose-une-plateforme-ludique-et

Stratégie régionale sur les perturbateurs endocriniens en Auvergne-Rhône-Alpes, 2025/11/04
Découvrez la stratégie régionale sur les perturbateurs endocriniens en Auvergne-Rhône-Alpes, portée par l'ARS et ses partenaires. Axée sur la sensibilisation et la facilitation du passage à l'action, elle s'adresse de nombreux acteurs : établissements de santé, collectivités, acteurs de la petite enfance, PMI... A travers ces professionnels relais, elle s'adresse aux parents
https://www.auvergne-rhone-alpes.ars.sante.fr/strategie-regionale-sur-les-perturbateurs-endocriniens-en-auvergne-rhone-alpes

Assessment of bisphenol-related knowledge and awareness among healthcare professionals: a cross-sectional analysis from Turkiye,
Aslan, E. and Kaplan, B., *Frontiers in Public Health*, Sep 12 2025, Vol. 13.

Background: A class of endocrine-disrupting chemicals with numerous industrial uses and proven harmful health effects are bisphenols, especially bisphenol A (BPA). These substances pose serious exposure risks in healthcare settings because they are widely found in consumer goods, food containers, and medical equipment. Even though there is growing evidence that exposure to bisphenols can cause metabolic, reproductive, and cardiovascular problems, little is known about these environmental toxins by medical professionals. One major obstacle to efficient risk assessment, patient counseling, and occupational safety implementation in clinical settings is the lack of awareness among frontline healthcare workers. Methods: The healthcare professionals at Gaziantep University & Scedil;ahinbey Research and Training Hospital participated in this descriptive cross-sectional study from April 15 to September 15, 2024. 397 healthcare professionals, including physicians, nurses, midwives, and health technicians, participated in standardized in-person interviews using a validated 13-item bisphenol knowledge assessment questionnaire. The data analysis was conducted using SPSS 25.0 software and included descriptive statistics, independent samples t-tests, one-way ANOVA, chi-square tests, Spearman correlation analysis, and CHAID decision tree analysis. Results: A critically low level of awareness was indicated by the fact that only 23.7% of participants reported having previously encountered bisphenols. With a mean knowledge score of 3.90 +/- 3.48 out of 13 possible points, 82.6% of healthcare professionals were classified as having inadequate knowledge ($p < 0.001$). A significant difference in knowledge was observed based

on professional title (physicians scored the highest, p = 0.015), marital status (married vs. single: 4.26 +/- 3.57 vs. 3.39 +/- 3.30, p = 0.014), and professional experience (6-10 years vs. 0-5 years: 4.29 +/- 3.48 vs. 3.30 +/- 3.15, p = 0.049). A positive correlation was observed between age and knowledge levels (r = 0.133, p = 0.008). Conclusion: The vast majority of Turkish healthcare professionals do not fully comprehend the sources of exposure, the health risks, or the precautions that should be taken about bisphenols, according to this study. These findings indicate that comprehensive educational interventions and policy reforms are urgently required to enhance environmental health literacy in healthcare settings. https://doi.org/10.3389/fpubh.2025.1627745

A comprehensive review of emerging environmental contaminants of global concern,
Boahen, E., Owusu, L. and Adjei-Anim, S. O., *Discover Environment*, Sep 16 2025, Vol. 3, no. 1.

Emerging contaminants (ECs) encompass a diverse range of synthetic and naturally occurring chemicals, including pharmaceuticals and personal care products (PPCPs), per- and polyfluoroalkyl substances (PFAS), endocrine-disrupting chemicals (EDCs), micro- and nano-plastics (MNPs), and biological agents.These contaminants have been increasingly detected in various environmental matrices due to increasing anthropogenic activities. Although not newly introduced, these substances have attracted growing scientific attention in recent years due to their potential ecological and human health impacts, coupled with advances in analytical methods that now allow detection at trace levels. This review presents a comprehensive synthesis of EC sources, environmental behavior, toxicological effects, and detection techniques. Analytical approaches such as gas chromatography (GC), high-performance liquid chromatography (HPLC), mass spectrometry (MS), and high-resolution tandem techniques (LC-MS/MS) have become central to EC identification and quantification. Additionally, molecular and biochemical tools, such as enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR), and biosensors, are proving essential in the detection of biologically active contaminants and pathogens. ECs have been implicated in endocrine disruption, antibiotic resistance, oxidative stress, and bioaccumulation in aquatic organisms, posing threats to food safety and public health. Although urban and industrial regions typically show higher contamination levels, pristine environments are also impacted due to long-range environmental transport processes. Understanding the fate and distribution of ECs is vital for crafting regulatory frameworks and sustainable management strategies. A multidimensional approach involving advanced analytical science, environmental monitoring, policy action, and public awareness is crucial to mitigate the rising threat of emerging contaminants globally. https://doi.org/10.1007/s44274-025-00259-x

The impact of chemical pollution and warming on male fertility: a narrative review by the Special Interest Group "Environment and Fertility" of the Italian Society of Fertility and Sterility and Reproductive Medicine (SIFES-MR),
Defeudis, G., De Angelis, C., Mazzilli, R., Barbagallo, F., Leanza, C., Sabovic, I., Condorelli, R. A., Rago, R., Gianfrilli, D., Pivonello, R., Di Nisio, A., Anserini, P., Foresta, C. and Italian Soc Fertility Sterility Reprod Med, S. M., *Journal of Assisted Reproduction and Genetics*, 2025.

Environmental changes are a growing global concern, and their impact on reproductive health remains incompletely understood. In this narrative review, conducted on behalf of the Italian Society of Fertility and Sterility and Reproductive Medicine (SIFES-MR), we examined the impact of the environment on male fertility, considering endocrine-disrupting chemicals (EDCs), air pollution, and global warming, with the aim of identifying strategies to improve reproductive outcomes. Scientific literature demonstrates that all these aspects may contribute to a decline in reproductive health, impairing sperm count, motility, and morphology as well as reducing testicular hormonal function. Future research should focus on the role of environmental factors in male hypogonadism, impaired

spermatogenesis, genital abnormalities, and transgenerational effects. https://doi.org/10.1007/s10815-025-03678-0

Membrane technologies for endocrine-disrupting chemical removal: A state-of-the-art review on materials, mechanistic insights, and future directions,
Lgaz, H., Zouhair, F. Z., Benkhaya, S., Lee, H. S. and Messali, M., *Separation and Purification Technology*, Feb 7 2026, Vol. 380.

Endocrine-disrupting chemicals (EDCs) pose critical environmental and public health challenges due to their persistence, bioactive nature and widespread presence in water systems. Membrane technologies have emerged as advanced solutions to effectively mitigate these contaminants. However, their optimal performance remains critically dependent on membrane selection, modification strategies, and a profound understanding of underlying separation and degradation mechanisms. This comprehensive review critically analyzes the state-of-the-art in membrane-based technologies, including microfiltration (MF), ultrafiltration (UF), nanofiltration (NF), reverse osmosis (RO), forward osmosis (FO), membrane bioreactors (MBRs), and advanced specialized membrane systems. Each membrane class is systematically evaluated for its efficacy in EDC removal, focusing on cutting-edge material innovations, hybrid configurations, and operational strategies. The mechanisms driving EDC rejection (size exclusion, electrostatic repulsion (Donnan exclusion), hydrophobic partitioning, adsorption, and catalytic degradation) are examined at a fundamental level, supported by detailed molecular and physicochemical insights. Notably, recent breakthroughs, including nanoconfined catalytic membranes, electro-assisted reactive systems, and biomimetic membrane architectures, are highlighted, offering significant enhancements in selectivity, permeability, fouling resistance, and catalytic performance. Critical research gaps are identified, emphasizing the need for targeted membrane nanoarchitecture engineering, precise molecular-level control of surface interactions, scalable catalytic integration, and robust operational performance under realistic environmental conditions. Finally, strategic future directions are proposed, envisioning transformative advancements through synergistic integration of nanotechnology, computational modeling, and sustainable membrane designs, ensuring that membrane technologies remain at the forefront in addressing emerging threats posed by endocrine-disrupting chemicals. https://doi.org/10.1016/j.seppur.2025.135218

Perturbateurs endocriniens et perception des risques avant, pendant et après la grossesse : une revue systématique de la littérature,
Musso, A., Chevalier, N., Bailly, L. and Pradier, C., *Gynécologie Obstétrique Fertilité & Sénologie*, 2025/11/01/ 2025, Vol. 53, no. 11, p. 622-623.

Objectif Colliger les expériences, représentations et perceptions des risques sur les perturbateurs endocriniens (PE) par la population avant, pendant la grossesse et en période postnatale. Thèmes peu explorés dans la littérature. Méthodes Revue de la littérature conduite selon la méthodologie PRISMA 2020 entre le 25/10/24 et le 01/11/24. Critères d'inclusion: tout type d'étude, sans limite de date de publication, dont les résumés et articles intégraux étaient accessibles, rédigés en français et en anglais à partir des bases de données Pubmed MEDLINE, Embase, Google Scholar qui mesuraient les représentations et risques perçus par la population sur les PE avant/pendant et après grossesse. Résultats 2603 occurrences obtenues à partir des équations de recherche. 6/2603 ont été incluses, publiées entre 2016 et 2024. 5/6 étaient françaises, 1 était coréenne. 1/6 était de méthodologie qualitative, 1/6 incluait 3 essais contrôlés randomisés, 2/6 avec méthodologies mixtes, 2/6 étaient quantitatives exclusives par questionnaires auto-administrés. 1/6 s'intéressait à la période pré conceptionnelle. Les effectifs étaient au maximum de 15 pour les méthodes qualitatives, de 300 pour celles quantitatives. Seules les femmes étaient concernées. Globalement, elles considéraient

être bien informées sur les PE, avec des variations de perception de dangerosité selon la molécule concernée. Elles estimaient que les dangers existaient pour elles-mêmes, surtout pour leur fœtus/enfant, minimisaient leurs expositions aux PE, reconnaissaient avoir besoin de plus d'informations fiables tôt dans la grossesse, mais avaient des niveaux d'anxiété plus élevés après sensibilisation. Conclusion Les interventions pour sensibiliser les femmes en période périnatale devraient prendre en compte la complexité des représentations que les PE évoquent tout comme les aspects anxieux qu'ils génèrent. Leur efficacité à long sur la réduction à l'exposition n'est pas évaluée. Les hommes ne sont pas interrogés. Cette revue de littérature est le point de départ d'une recherche doctorale sur la prévention/diminution de l'exposition aux PE en période préconceptionnelle et pernatale chez les femmes et les hommes avec mesures des changements de comportements, freins, motivations et objectivations biologiques.
https://doi.org/10.1016/j.gofs.2025.09.041

Taxation de l'hexane : comprendre la controverse avec Guillaume Coudray,
O'gomes, I. D., *Sciences et Avenir*, 2025/11/10

Samedi 8 novembre, les députés ont voté une taxe sur l'hexane, un solvant utilisé pour extraire les huiles végétales et suspecté d'être nocif pour la santé à long terme. Guillaume Coudray nous explique les enjeux derrière ce vote. https://doi.org/,
https://www.sciencesetavenir.fr/nutrition/hexane-un-solvant-sur-la-sellette-le-decryptage-de-guillaume-coudray-apres-le-vote-des-deputes_189243

Le plus grand groupe chimique mondial abandonnera définitivement les PFAS, ces produits chimiques appelés « polluants éternels » d'ici 2028
Res (2025). Réseau Environnement Santé.
Les fabricants commencent à abandonner progressivement la production de PFAS. Les grandes entreprises chimiques ont discrètement commencé à abandonner la production des «polluants éternels » alors que le risque de poursuites judiciaires augmente et que l'UE envisage d'imposer des restrictions importantes à leur utilisation. Le groupe de produits chimiques connus sous le nom de PFAS, https://www.reseau-environnement-sante.fr/le-plus-grand-groupe-chimique-mondial-abandonnera-definitivement-les-pfas-ces-produits-chimiques-appeles-polluants-eternels-dici-2028/

Pesticides, an urgent challenge to global environmental health and planetary boundaries,
Vandenberg, L. N., Pierce, E. J. and Arsenault, R. M., *Frontiers in Toxicology*, Oct 3 2025, Vol. 7.

There is increasing evidence that pesticides act as endocrine disruptors, developmental toxicants, and reproductive toxicants. In this review, we describe several global challenges associated with pesticide production and use that put the health of human and wildlife populations at risk. These include: (1) the global production and use of pesticides is high, leading to increasing rates of release into the environment; (2) exposures to non-target species (including humans) are well documented, and pesticides often have adverse effects on these species; (3) pesticides, and especially those that are persistent organic pollutants, do not stay where they are used, contributing to ecosystem pollution far from their intended areas of application; (4) climate change can exacerbate the use of pesticides; and (5) social determinants of health (race/ethnicity, sex, and occupation) influence pesticide exposures and the adverse effects associated with these exposures. In 2009, the concept of planetary boundaries was introduced as a framework to evaluate how human actions impact earth systems. The planetary boundaries were based on a shared understanding that human activities have significant and sometimes irreversible effects on key aspects of environmental health. When considering the global impact of pesticides, these products can disrupt several planetary boundaries including biogeochemical cycles, biosphere integrity (e.g., measures of biodiversity), and the

availability of clean freshwater, but the greatest challenge posed by pesticides is the "novel entities" boundary (i.e., the introduction of synthetic chemicals and materials into the environment). The planetary boundaries framework makes clear that failure to act against the most concerning chemicals, including pesticides, ultimately puts the survival of human populations at risk.
https://doi.org/10.3389/ftox.2025.1656297

Environmental Chemicals and Female Reproductive Health: Unraveling Mechanisms and Societal Impacts - A Narrative Review,
Xie, Y. D., Peng, R. T. and Xiao, L., *Clinical and Experimental Obstetrics & Gynecology*, Jul 31 2025, Vol. 52, no. 8.

Objectives: To examine the impacts of environmental chemicals on female reproductive health, identify key mechanisms of reproductive toxicity, and discuss potential strategies to mitigate these effects.Mechanism: Environmental chemicals such as per- and polyfluoroalkyl substances, heavy metals, pesticides, microplastics, quaternary ammonium compounds, and other pollutants, disrupt the hypothalamic-pituitary-gonadal axis (HPG), impair ovarian function, and contribute to reproductive dysfunction through mechanisms such as oxidative stress, hormonal disruption, and epigenetic modifications.Findings in Brief: These chemicals contribute to menstrual irregularities, infertility, and pregnancy complications. They also increase the risk of reproductive system disorders, including endometriosis, polycystic ovary syndrome (PCOS), and ovarian cancer. Additionally, transgenerational effects mediated by epigenetic modifications, germ cell damage, and placental transfer may adversely affect offspring health, increasing the risk of reproductive dysfunction, neurodevelopmental disorders, metabolic diseases, and cancer.Conclusions: Despite growing evidence, significant knowledge gaps remain in understanding the mechanisms of reproductive toxicity, identifying biomarkers for early detection, and assessing the long-term effects of low-dose, chronic exposure. Addressing these challenges requires stricter regulations, the development of safer chemical alternatives, public awareness campaigns, and continued research to safeguard reproductive health for current and future generations.
https://doi.org/10.31083/ceog39882

Toxicité sur les animaux

Perinatal exposure to BPA leads to pronounced prostatic morphophysiological disorders in a rodent model of induced hyperplasia,
Bicalho-Silva, S., Grigio, V., Ruiz, T. F. R., Calmon, M. D., Rahal, P., Taboga, S. R., Dos Santos, F. C. A. and Vilamaior, P. S. L., *Molecular and Cellular Endocrinology*, Dec 1 2025, Vol. 610.

Bisphenol A (BPA) is a ubiquitous endocrine disruptor potentially harmful to male reproductive health. We aimed to investigate the impacts of perinatal exposure to a historically relevant and realistic dose of BPA on the ventral prostate under normal conditions and with prostatic hyperplasia in Mongolian gerbils (Meriones unguiculatus). Females were exposed to BPA (50 mu g/kg/day) during gestation and lactation. The F1 male offspring were maintained until adulthood and subsequently treated with testosterone to induce prostatic hyperplasia. Morphological, molecular, and hormonal parameters were assessed on the ventral prostate. Testosteronesupplemented gerbils showed increased epithelium height and smooth muscle layer thickness. In the context of hyperplasia, perinatal exposure to BPA led to the onset of severe histopathologies (e.g., prostatic intraepithelial neoplasia, adenocarcinoma, and microacini), associated with increased cell proliferation. Perinatal BPA-exposed gerbils with prostatic hyperplasia showed increased pro-

inflammatory markers (e.g., IL-6, COX-2, and F4/80), followed by a reduction in IL-10 protein levels. Regarding the steroid receptors, gerbils from this group presented a decrease in AR, followed by an increase in epithelial ER alpha expression. Molecularly, ER beta protein levels were higher in the prostate of perinatally exposed to BPA or testosterone-supplemented gerbils. Moreover, serum testosterone and estradiol levels increased after testosterone supplementation, whereas the T/E2 ratio increased in gerbils exposed to both treatments. Overall, the current study presents novel and comprehensive data on the life-long morphophysiological disorders caused by perinatal exposure to BPA on the ventral prostate of gerbils, highlighting the pronounced impacts observed in the context of hyperplasia. https://doi.org/10.1016/j.mce.2025.112664

Endocrine effects of Imazalil on aromatase expression, vitellogenesis and ovarian histology using cyp19a1a-eGFP-casper transgenic zebrafish,
De Oliveira, J., Ly, T. K., Chadili, E., Thermes, V., Mergot, A., Piccini, B., Palluel, O., Budzinski, H., Le Menach, K., Pardon, P., Beaudouin, R., Cousin, X., Brion, F. and Hinfray, N., *Aquatic Toxicology*, Dec 2025, Vol. 289.

Considering the hazards and risks posed by endocrine disrupting chemicals (EDC) to organisms, there is a need to study their effects. To that end, transgenic fish are powerful models that can provide mechanistic information regarding the endocrine activity of test chemicals. In this study, we used a newly developed transgenic zebrafish line (cyp19a1a-eGFP-casper) in the OECD 21-day fish assay (OECD TG 230) to provide additional mechanistic insight on Imazalil (IMZ; 1.9; 9.9 and 140.7 mu g/L). After 21 days of exposure to IMZ, the circulating concentrations of 17-beta-estradiol (E2) and vitellogenin decreased in females, reflecting the aromatase activities inhibition. Exposure to 140.7 mu g/L of IMZ for 21 days also resulted in a change in the proportion of the different oocyte stages in the ovaries, with an accumulation of large oocytes in exposed females. In addition to the classical endpoints, in vivo GFP fluorescence was quantified in the ovaries during the time course of the exposure to follow gonadal aromatase expression. After seven days of exposure, ovarian aromatase expression increased in females exposed to medium and high concentrations of IMZ, persisting over the 21-day of exposure in fish from the highest concentration group and reflecting a compensatory response to the aromatase enzymatic activities inhibition. Results from the present study provided valuable information on the mode of action and the effects of IMZ in zebrafish. Transgenic zebrafish exposure to IMZ caused a cascade of responses consistent with effects reported for wild-type fish exposed to azole fungicides, both qualitatively and quantitatively. The cyp19a1a-eGFP (-casper) transgenic zebrafish lines, allowed in vivo monitoring of gonadal aromatase expression in a time-and concentration-dependent manner thereby demonstrating their relevance to provide complementary mechanistic information on aromatase in regulatory assays such as OECD TG 230. https://doi.org/10.1016/j.aquatox.2025.107580

Influence of perinatal exposure to an endocrine disruptor mixture on the renal microenvironment of aged male rat offspring: histopathological aspects,
Dolfini, P. M., Hinokuma, K. D., Nai, G. A., Castilho, A. C. D. and Mendes, L. D., *Journal of Developmental Origins of Health and Disease*, Sep 1 2025, Vol. 16.

The developmental origins of health and disease hypothesis suggests that environmental exposures during critical developmental windows increase the risk of disease later in life. Among these, endocrine disruptors (EDs) are particularly concerning due to their ubiquitous presence. The kidneys are highly susceptible to EDs toxicity during the perinatal period; however, long-term effects of ED mixtures on renal structure in aging remain unclear. This study aimed to characterize the renal histoarchitecture of aged rats after perinatal exposure to an ED mixture. Pregnant Sprague-Dawley rats were assigned to two groups: Control (corn oil, 2 ml/kg) and ED Mix (32.11 mg/kg/day of 12

EDs, including phthalates, pesticides, UV filters, bisphenol A, and butylparaben, in corn oil). Exposure occurred from gestational day 7 to postnatal day 21. Offspring were euthanized at postnatal day 440. ED mixture exposure did not affect the organosomatic index. However, ED Mix offspring presented renal lesions, including necrosis and tubular fusion, with a trend toward increased pathological changes. Morphometric analysis revealed enlarged nuclei and increased nuclear perimeters in the cortex and medulla, along with altered cellular organization in glomerular and medullary regions. Collagen organization was disrupted, with increased fibrosis in cortical and medullary compartments and reduced collagen type I and III in glomeruli. These findings indicate that perinatal exposure to an ED mixture alters nuclear phenotype and promotes extracellular matrix remodeling in distinct renal compartments. Such changes suggest long-term impacts on renal structure and function, emphasizing the health risks associated with early-life exposure to complex ED mixtures. https://doi.org/10.1017/s2040174425100172

Androgen receptor antagonist flutamide modulates estrogen receptor alpha expression in distinct regions of the hypospadiac rat penis,
Elmelund, E., Draskau, M. K., Berg, M., Strand, I. W., Black, J. R., Axelstad, M., Pask, A. J. and Svingen, T., *Frontiers in Endocrinology*, Sep 12 2025, Vol. 16.

Introduction Intrauterine exposure to endocrine disrupting chemicals (EDCs), particularly anti-androgens, has been implicated in hypospadias by disrupting fetal masculinization of the genital tubercle (GT). Other pathways, including estrogen signaling, may also contribute but remain poorly characterized, especially in rats - a key model in chemical toxicity testing. Estrogen signaling has also been linked to hypospadias in mice, raising questions about androgen-estrogen interactions in guiding GT differentiation.Methods We induced hypospadias in male rat offspring via intrauterine exposure to the antiandrogenic drug flutamide and characterized androgen and estrogen receptor expression.Results We observed key structural and transcriptional changes in the developing penis, including altered estrogen receptor a (ERa, Esr1) expression. Notably, beyond this established androgen-estrogen relationship in hormone-sensitive tissues, anti-androgenic exposure also induced spatial changes in Esr1 expression in specific regions of the GT.Discussion Future toxicological testing using new approach methodologies (NAMs) should consider androgen-estrogen balance and crosstalk in reproductive tissues as a mechanism of action.
https://doi.org/10.3389/fendo.2025.1654965

Perinatal neurodevelopmental effects of endocrine disruptors: Insights from metabolome mapping in the rat hippocampus,
Evangelista, S., Lichtensteiger, W., Schlumpf, M., Rancan, L., Paredes, S. D., Linillos-Pradillo, B., Lamoree, M. H. and Leonards, P. E. G., *Toxicology*, Dec 2025, Vol. 518.

Metabolism is critical for neurodevelopment, yet the mechanisms by which endocrine-disrupting chemicals (EDCs) contribute to neurodevelopmental disorders remain poorly defined. Using a rat model, we investigated hippocampal metabolomic responses at postnatal day 6 following maternal exposure to six structurally diverse EDCs (bisphenol F, permethrin, butyl benzyl phthalate, triphenyl phosphate, perfluorooctane sulfonic acid, and DINCH) from pre-mating through lactation. Targeted steroid, thyroid, and neurosteroid hormones, neurotransmitters, and untargeted lipidomics were profiled to map disrupted pathways. The analysis revealed sex-specific, chemical-specific, and shared metabolic signatures of developmental neurotoxicity. Key affected endpoints across chemicals included corticosterone, pregnenolone sulfate, and N-acylethanolamine lipids, confirming hormonal disruption while uncovering novel non-EATS (estrogen, androgen, thyroid, and steroidogenesis) pathways and mechanisms of action. These findings provide new insights into EDC-mediated disruption of hippocampal development and identify potential molecular biomarkers that

may support future mechanistic research and chemical risk assessment. https://doi.org/10.1016/j.tox.2025.154281

Benzophenone-3 (BP3), bisphenol A (BPA), and their combination impair ovarian response to gonadotropin stimulation in a multi-exposure multiparity model,
Galliani, V., Fessia, J., Santamaria, C. G., Abud, J. E. and Rodriguez, H. A., *Environmental Toxicology and Pharmacology*, Oct 2025, Vol. 119.

Despite prevailing evidence that endocrine-disrupting chemicals (EDCs) may exert effects across multiple pregnancies, most studies focus on the first pregnancy Using a multiparity murine model, we evaluated the effects of benzophenone-3 (BP3), bisphenol-A (BPA) or the combination (BP3 +BPA) exposure over two gestational periods (P1 and P2) on pregnancy outcomes and the gonadal function in female offspring from each pregnancy. While maternal weight, litter size, and sex ratio were unaffected, gestation length was altered in BPA and BP3 +BPA groups both in P1 and P2. Ovulation was affected in P2 offspring in all EDC exposed groups. Notably, antral follicle numbers were reduced in all exposed groups, while BPA and BP3 +BPA exposure diminished the primordial follicle reserve in P2 offspring. Estradiol levels were elevated in P2 offspring in the BP3 +BPA group with hCG stimulation. These findings highlight the importance of considering cumulative exposure and exposure to combinations of BP3 and BPA when assessing the long-term reproductive effects of EDCs. https://doi.org/10.1016/j.etap.2025.104821

Concentration-Related Ultrastructural Alterations in Mouse Oocytes Following In Vitro Lindane Exposure,
Gatti, M., Belli, M., De Rubeis, M., Nottola, S. A., Macchiarelli, G., Tatone, C., Di Emidio, G. and Palmerini, M. G., *Applied Sciences-Basel*, Jul 26 2025, Vol. 15, no. 15.

Lindane, a persistent organochlorine pesticide, exerts toxic effects on the female reproductive system, compromising oocyte quality and maturation. However, the effects of this pesticide on mammalian oocyte morphology and ultrastructure remain unknown. This study investigated the effects of Lindane on mouse oocyte ultrastructure using an in vitro model with Transmission Electron Microscopy (TEM) at concentrations from 1 to 100 mu M. The results revealed a progressive dose-related trend of alterations: at 1 mu M, mild swelling of smooth endoplasmic reticulum (SER) vesicles; at 10 mu M, increased SER dilation and cytoplasmic disorganization; and at 100 mu M, pronounced vacuolization, mitochondrial swelling, dense lamellar bodies (dlbs), and multivesicular bodies (MVBs) indicative of autophagic activity. Mitochondrial alterations increased significantly with concentration: 3.2 +/- 0.8 (control), 5.7 +/- 1.0 (1 mu M), 9.4 +/- 1.5 (10 mu M), and 16.8 +/- 2.3 (100 mu M) altered mitochondria per oocyte ($p < 0.01$). Vacuole frequency was notably elevated at 100 mu M (4.3 +/- 1.1 vs. 0.7 +/- 0.5 in controls), and mislocalization of organelles within the ooplasm was observed. In conclusion, Lindane-induced oocyte ultrastructural alterations were observed at all tested concentrations but were more pronounced at 100 mu M. These results highlight its impact on female fertility and may guide the search for protective agents, as well as efforts to reduce environmental exposure to endocrine disruptors. https://doi.org/10.3390/app15158320

Exposure to Kalach, a Glyphosate-Based Herbicide, During Pregnancy and Lactation Induces Hypothyroidism and Bone Disorders in Rat Offspring,
Hamdaoui, L., El Feki, H., Ben Amor, M., Oudadesse, H., Atwan, M., Alshammari, A. M., Brahmi, F., Ben-Nasr, H., Badraoui, R. and Rebai, T., *Toxics*, Sep 4 2025, Vol. 13, no. 9.

Kalach (KL) is a glyphosate (G)-based herbicide extensively used in agricultural and urban areas in Tunisia. It has been reported that G crosses the placenta in pregnant rats, potentially disrupting organ function in offspring. The present study examined the effects of prenatal and lactational exposure to KL on thyroid function, bone integrity, and phosphocalcic homeostasis in rat offspring. Pregnant rats were divided into two groups, group A (control group) and group B, exposed to KL (each mother rat received 0.07 mL of KL diluted in 1 mL of water by gavage). On postnatal day 14, plasma samples were analyzed for thyroid hormones, calcium, and phosphorus. Histology and immunohistochemical study of bone and thyroid, Fourier-transform infrared (FTIR) spectroscopy, X-ray diffraction (XRD), and scanning electron microscopy assessed alterations. Additionally, we complemented the in vivo study with an in silico study. We found that KL induced hypothyroidism, necrosis in thyroid tissue, and phosphocalcic imbalance, leading to skeletal abnormalities. Structural and mineralization defects in bone were confirmed by FTIR and XRD analysis. The in silico study revealed that G bids to growth hormone receptors and thyroglobulin with good affinity, corroborating the in vivo findings. In conclusion, KL may interfere with bone tissue, growth hormone receptors, and thyroglobulin, impair hypothyroidism, and function as an endocrine disruptor exposure. Consequently, KL induces disorganization of the femoral growth plate.
https://doi.org/10.3390/toxics13090752

Pesticide-induced epigenetic suppression of WNT signaling and NF-κB-driven inflammation impairs ovarian function in rats,
Jan, J., Sheikh, W. M., Gul, S., Mohidin, R., Bhat, O. M., Lone, M. N., Shah, S. A., Dar, A. H., Zargar, M. A., Bashir, S. M. and Wani, N. A., *Food and Chemical Toxicology*, Nov 2025, Vol. 205.

The study examined the impact of chlorpyrifos, dimethoate, and their co-exposure on ovarian structure and function in female Wistar rats. The study involved 24 rats, divided into four groups: control, chlorpyrifos (3 mg/kg), dimethoate (30 mg/kg), and combination. Histopathology revealed degenerated and atretic follicles, disorganized granulosa cells and cystic follicles in pesticide exposed rats. Hormonal analysis showed decrease in FSH, LH, PG, T and AMH and increase in ED levels. Gene expression studies revealed significant upregulation of ESR2 (similar to 2, similar to 1.8, and similar to 1.85 fold respectively) in chlorpyrifos, dimethoate and combination groups. In contrast, RSPO2, WNT7A, WNT3A and WNT5A were downregulated (reduced by similar to 1.73-1.8, 1.7-2.6, 1.45-2.13 and 1.3-1.75 fold, respectively). The changes correlated with reduced beta-catenin activation. DNA methylation analysis revealed an inverse correlation between methylation and gene expression, alongside upregulation of DNMT3A and DNMT3B (similar to 4.5, similar to 2.1, similar to 4.9; similar to 3.75, similar to 2.2, similar to 3.8 fold in chlorpyrifos, dimethoate and combination groups respectively), suggesting methylation-mediated repression. Furthermore, enhanced expression of inflammation-related genes and cytokines, coupled with NF-kappa B activation, indicated significant inflammatory responses. Overall, the findings highlight gene specific DNA methylation and inflammatory disruptions in pesticide-exposed ovaries. However, the lack of ChIP assay limits confirmation of DNMT recruitment, which should be addressed in future studies.
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The effects of bisphenol compounds on endocrine disruption and reproductive function from epidemiological analysis to animal exposure: A mixture analysis,
Jiang, P. Y., Wang, W. W., Li, J. D., Li, Y. T., Ji, X. T. and Yue, H. F., *Journal of Environmental Sciences*, Feb 2026, Vol. 160, p. 537-547.

Bisphenol F (BPF) and Bisphenol S (BPS) are widely used substitutes for Bisphenol A (BPA). However, growing evidence indicated that BPF and BPS may induce physiological effects similar to those of BPA. Furthermore, chemical management and control is primarily focus on the risk assessment of

individual compounds, often overlooking the implications of chemical mixtures. We hypothesize that exposure to a mixture of BPA and its substitutes will enhance their endocrine-disruptive effects, disrupt steroid hormone homeostasis, and further impair reproductive system functionality. In the animal study, both female and male mice were exposed to 333 mu g/kg of BPA, BPF, BPS, their mixture (333 mu g/kg (MIXL), and 1 mg/kg (MIXH)) via gavage daily for four weeks. The study demonstrated that bisphenols (BPs) affected the expression of genes related to steroid hormone synthesis. The MIXL group of female mice exhibited an increasing trend in estradiol (E2) levels and a decreasing trend in progesterone (Pg) and testosterone (TT) levels. Additionally, follicular development was impacted, resulting in an increased number of atretic follicles. In contrast, a significant increase in E2 concentration and disruption of testicular morphology were observed in the MIXH group of male mice, accompanied by a decline in sperm quality. Importantly, these results were corroborated by a population-based investigation. Collectively, the animal experiments indicate that mixed exposure to BPs disrupts hormone levels and adversely affects reproductive function, while epidemiological evidence further establishes correlative links between bisphenols and hormone levels. These findings underscore the necessity of considering chemical mixtures during testing and risk assessment. https://doi.org/10.1016/j.jes.2025.04.042

Integrated transcriptome analysis of rats exposed to bisphenol mixtures from the fetal to developmental stage,
Jung, S., Quah, Y., Ham, O., Kim, S., Jeong, J. S., Kim, W., Lee, S. J. and Yu, W. J., *Toxicology Research*, Aug 2025, Vol. 14, no. 4.

Bisphenol A (BPA), widely used in plastics and resins, has raised health concerns for its endocrine-disrupting effects. BPA analogues such as bisphenol S (BPS) and bisphenol F (BPF) emerged as alternatives but exhibit similar risks. Despite regulations on BPA in many countries, alternatives remain insufficiently controlled. Although the safety of BPS and BPF has not been sufficiently verified, these compounds have already been detected in various environmental sources and human urine, raising serious concerns. While bisphenols are expected to have various adverse effects, research remains limited. This study investigates the adverse effects of bisphenols mixture on rats from fetal stage to young adulthood by analyzing transcriptomes in multiple tissues-liver, kidney, thyroid gland, and reproductive organs-and by gender, to identify key genes affected by bisphenol exposure. Dams were orally administered test substances from gestational day 6 to lactation day 6, and F1 pups received the same substances at half the concentration from postnatal day 7 to day 63. Transcriptome analysis of the collected tissues identified core genes related to high-density lipoprotein metabolism and hormone secretion, providing insights into mechanisms through which BPA may disrupt hormonal balance. Furthermore, the study suggests that combined exposure to BPA, BPS, and BPF produces distinct effects compared to BPA alone, with pronounced impacts on the thyroid and reproductive organs, despite individual concentrations being below the no-observed-adverse-effect-level. These findings highlight the potential cumulative impact of endocrine disrupting chemicals in the body. https://doi.org/10.1093/toxres/tfaf120

Effects of TBBPA Exposure on Neurodevelopment and Behavior in Mice,
Kim, Y., Hwang, I., Kim, S. and Jeung, E. B., *International Journal of Molecular Sciences*, Jul 28 2025, Vol. 26, no. 15.

Tetrabromobisphenol A (TBBPA) is a brominated flame retardant widely used in consumer products. TBBPA is often detected in soil, water, organisms, and even in human blood and breast milk. Hence, it is accessible to developing fetuses and nursing offspring after maternal exposure. The reported evidence for the endocrine disruption of TBBPA in the brain has raised concerns regarding its effects on neurodevelopmental and behavioral functions. This study investigated the effects of TBBPA

exposure on neurodevelopment. A cell-based developmental neurotoxicity assay was performed to determine whether TBBPA is a developmental neurotoxicant. The assay revealed TBBPA to be a developmental neurotoxicant. C57BL/6N maternal mice were administered TBBPA at 0, 0.24, and 2.4 mg/kg during pregnancy and lactation, and their offspring underwent behavioral testing. The behavioral experiments revealed sex-specific effects. In females, only a deterioration of the motor ability was observed. In contrast, deteriorations in motor function, memory, and social interaction were noted in males. Furthermore, we validated changes in the expression of genes associated with behavioral abnormalities, confirming that perinatal exposure to TBBPA, at the administered doses, can affect neurodevelopment and behavior in offspring. These findings highlight the need for more in-depth and multifaceted research on the toxicity of TBBPA. https://doi.org/10.3390/ijms26157289

Implications of a combined perinatal exposure to BPA and BP-3 for offspring folliculogenesis and ovarian function in mice,
Krieger, E., Fischer, F., Howanski, J., Wagner, M., Romanelli, F., Fink, B., Bauer, M., Schumacher, A., Kretschmer, T. and Zenclussen, A. C., *Ecotoxicology and Environmental Safety*, Sep 1 2025, Vol. 302.

Endocrine disrupting chemicals (EDCs), like bisphenol A (BPA) and benzophenone-3 (BP-3), can interfere with hormone systems, posing risks to fertility and reproduction. Exposure to EDCs is unavoidable making it a relevant environmental health topic, however the impact of real-life EDC mixtures is largely unknown. This study explored the effects of a combined BPA and BP-3 exposure at tolerable intake levels for humans during pregnancy and early life on ovarian development and function in an established mouse model. Mice were daily exposed to concentrations of 4 mu g/kg BPA orally, 50 mg/kg BP-3 dermally, and the combination of BPA+BP-3 through gestation and lactation, a susceptible developmental period. Female offspring of BPA and BP-3 exposed mice exhibited increased birth weight and elevated bodyweight by postnatal day 7. By day 30, after hormonal stimulation to induce ovulation, exposed offspring showed disrupted ovarian follicle maturation and altered ovarian response to stimulation with exogenous gonadotropins. Moreover, the number of NK cells rose in the ovaries, and genes linked to hormone signaling, hormone synthesis, and ovarian tissue remodeling were altered relative to unexposed controls. These findings suggest that early life exposure to BPA and BP-3 at environmentally relevant doses impairs ovarian development and function in mice indicating that immune cells and hormonal signaling in the ovaries are targets of endocrine disruptors at relevant concentrations. Such endocrine disruption may be compromising fertility and reproductive health in later life. Our research underscores the importance of investigating the impact of combined EDC exposure on the reproductive system. https://doi.org/10.1016/j.ecoenv.2025.118750

Imidacloprid actions in the mouse mammary gland structure and epithelial mammary cells. Role of GPER and nAChR,
Leguizamón, M. A., Buján, S., Sánchez, Y., Pontillo, C., Chiappini, F., Español, A., Randi, A. and Miret, N., *Environmental Research*, Nov 15 2025, Vol. 285.

The neonicotinoid imidacloprid (IMI) is used worldwide for insect control and represents a potential risk to populations, due to its potential action as an endocrine disruptor (ED). IMI binds to the postsynaptic nicotinic acetylcholine receptor (nAChR), whereas other neonicotinoids can activate the G protein-coupled estrogen receptor (GPER). Here, we examined the IMI effect on the mammary gland in a peripuberal model where female mice were exposed to IMI (0.01, 0.1 and 10 mg/kg/day). Alterations observed in the mammary morphology included an increase in transverse ductal growth at 0.1 and 10 mg/kg/day and a reduction in branch density at 0.1 mg/kg/day. Furthermore, 10 mg/kg/day IMI increased the number of terminal end buds (TEBs), induced ductal hyperplasia and epithelial cell proliferation. In mammary epithelial NMuMG cells, IMI (0.01-10 mu M) showed no

cytotoxic effect but boosted clonogenic capacity at 0.1 and 1 mu M. Western blot findings revealed that 1 and 10 mu M IMI rises GPER and aromatase expression, but declines progesterone receptor levels at all assayed doses. IMI (10 mu M) also increased alpha 7-nAChR expression at 24 h and induced c-Src phosphorylation after 1 h of treatment. Finally, 10 mu M IMI promoted cell migration and the proteolytic activity of metalloproteinase (MMP)-2 and-9 through GPER, alpha 7-nAChR, and c-Src. In summary, IMI promotes preneoplastic lesions and TEBs retention and increases mammary epithelial cell motility through GPER and alpha 7-nAChR. Our results support the hypothesis that IMI acts as an ED, affecting mammary gland structure. https://doi.org/10.1016/j.envres.2025.122620

The Physiopathological Link Between Bisphenol A Exposure and Molar Incisor Hypomineralization Occurrence: A Systematic Review,
Mathonat, E., Canceill, T., Marty, M., Prosper, A., Vinel, A. and Noirrit-Esclassan, E., *Dentistry Journal*, Jul 22 2025, Vol. 13, no. 8.

Objective: This study aimed to assess, through a systematic review, the potential link between bisphenol A (BPA) exposure and molar incisor hypomineralization (MIH). Methods: A systematic review was performed according to the PRISMA grid. All international studies-in vitro, in vivo, or clinical-evaluating the relationships between bisphenol A and MIH were included. An iterative search of eligible publications was conducted on May 26, 2025, using three different databases: PubMed, Science Direct, and Google Scholar. Results: Eleven studies were included in the review, ten of which were experimental studies. They were published between 2013 and 2024. Among the selected articles, a rat model was used in eight studies and seven established a link between MIH and BPA (63.64% of the articles). In the included studies, the incisors of rats treated with BPA presented asymmetrical white spots at the enamel level, with a phenotype similar to human MIH. The authors highlight the hypothesis of the implication of steroid receptors expressed by ameloblasts, in particular at the stage of maturation, thus impacting enamel quality. Conclusions: The results presented in this review highlight a trend in the interaction of bisphenol A with steroid receptors, thus affecting enamel quality. However, these associations are weak, and future studies should investigate cofactors modulating BPA's role in the development of MIH.
https://doi.org/10.3390/dj13080332

Transcriptomic Changes Across the HPG Axis Following Prenatal Exposure to the EDC Mixture NeuroMix,
Milewski, T. M., Streifer, M., Thompson, L. M., Sheinhaus, D., Hynes, A. and Gore, A. C., *Endocrinology*, Oct 2025, Vol. 166, no. 10.

Endocrine-disrupting chemicals (EDCs) are exogenous chemicals that are ubiquitous in our environment and found in everyday items. We previously reported that prenatal exposure of rats to a human-relevant mixture of EDCs, NeuroMix (NMX), led to alterations in physiological and behavioral phenotypes. Here, we used hypothalamic-pituitary-gonadal (HPG) tissues from these same male and female rats and conducted 3 ' Tag-based RNA sequencing (TagSeq) to investigate underlying molecular mechanisms. TagSeq revealed unique tissue- and sex-specific differentially expressed genes (DEGs). In males, among the HPG tissues, NMX had the greatest effects in the hypothalamic arcuate nucleus (ARC), with 613 DEGs. Gene ontology (GO) enrichment analysis revealed that genes upregulated in the ARC of NMX males were involved in synaptic plasticity, while genes downregulated related to responses to estradiol and glucocorticoids. In females, prenatal NMX exposure induced the largest transcriptome change in the ovaries, with 1295 DEGs. GO-enrichment analysis revealed upregulation of genes involved in cilium organization and movement, while genes downregulated in this region were related to immune-related processes. Using Qiagen Ingenuity Pathway Analysis, we identified the beta-estradiol pathway to be activated in all NMX

female tissues and the NMX male pituitary, and inhibited in NMX male ARC, ventromedial nucleus, and testes. To our knowledge, this is one of the first studies to conduct transcriptomic profiling across HPG tissues, with these results demonstrating that prenatal exposure to NMX affects gene expression across the HPG axis in a sex-dependent manner.
https://doi.org/10.1210/endocr/bqaf135

Maternal exposure to tributyltin alters female reproductive system development,
Miranda, R. A., Da Silva, B. S., Bertasso, I. M., De Souza, L. L., Maas, E., Graceli, J. B., Miranda-Alves, L., De Moura, E. G. and Lisboa, P. C., *Journal of Endocrinology*, Aug 1 2025, Vol. 266, no. 2.

Tributyltin (TBT) is a toxic compound used in antifouling paints and known for its endocrine-disrupting properties, including female reproductive dysfunction. We hypothesized that TBT exposure during gestation and lactation induces long-term reproductive alterations in female offspring. Pregnant Wistar rats were orally exposed from gestational day 7 to the end of lactation to 0.01% ethanol (control), TBT 100 ng/kg, or TBT 1000 ng/kg body weight. Female offspring were evaluated at postnatal days (PND) 21, 45, and 180 for biometric, hormonal, and ovarian parameters. Birth weight was reduced in the TBT100ng group, and body weight was reduced by PND180 in the TBT1000ng group. At PND45, testosterone increased in both TBT groups, while FSH decreased in the TBT100ng group. Estrous cyclicity irregularities, such as a prolonged metestrus-diestrus phase, were noted in the TBT1000ng group. Ovarian analysis showed increased cystic and atretic follicles at PND21 and PND45. Reduction in primordial follicles (TBT100ng) and corpora lutea (both TBT groups) was observed at PND180, along with ovarian fibrosis. TBT exposure led to age- and dose-dependent disruptions in ovarian follicle dynamics: initial increases in healthy follicles at PND21, followed by elevated unhealthy follicles and reduced healthy ones at later stages. At PND21, both TBT doses increased ER alpha expression, while TBT100ng increased AR expression. These changes were accompanied by a persistent increase in ovarian mast cells and elevated IL-6 protein expression, particularly at PND21 and PND180. Thus, maternal TBT exposure disrupts ovarian development and function, potentially increasing susceptibility to abnormal conditions such as polycystic ovary syndrome and primary ovarian insufficiency later in life.
https://doi.org/10.1530/joe-24-0357

Elucidating the impact of persistent organic pollutants on male reproductive health and testicular structure,
Ray, S. S., Gupta, P., Mahapatra, A., Suman, A. and Singh, R. K., *Toxicology Letters*, Aug 2025, Vol. 411, p. 37-49.

Persistent organic pollutants (POPs) are environmental contaminants that pose significant health risks due to their widespread distribution. This study examines the effects of POPs on male reproductive health using realistic human exposure scenarios. Male mice exposed to 28 ng of POPs for 35 days exhibited detrimental effects on sperm motility and count, significant changes in germ cell composition, and compromised steroidogenesis. Histopathological analyses revealed testicular architecture alterations and abnormal lipid accumulation in the interstitial space, potentially hindering steroidogenesis and Leydig cell function. Western blot and immunofluorescence studies showed reduced levels of steroidogenic markers. Flow cytometry indicated a decrease in round spermatids, suggesting impaired spermatogenesis. Molecular investigations revealed reduced mRNA expression of critical steroidogenic enzymes, while increased apoptotic markers and DNA fragmentation suggested apoptosis as a mechanism. This study highlights the need for stricter regulations and improved environmental health policies to mitigate the adverse effects of POPs on male reproductive health. https://doi.org/10.1016/j.toxlet.2025.07.002

Reproductive Effects of Endocrine Disruptors in Domestic Ruminants: Integrating In Vitro and In Vivo Evidence,
Sapanidou, V. G., Lavrentiadou, S. N. and Tsantarliotou, M. P., *Animals*, Sep 16 2025, Vol. 15, no. 18.

Endocrine-disrupting chemicals (EDCs) have raised increasing concern due to their potential effects on reproductive health. This review focuses on the impact of EDCs, particularly bisphenol A (BPA) and its analogues, and per- and polyfluoroalkyl substances (PFAS), on domestic ruminants (cattle and sheep) by integrating findings from both in vitro and in vivo studies. The analysis highlights how exposure to EDCs affects steroidogenesis, oxidative stress responses, apoptosis, epigenetic regulation, and overall fertility markers, such as oocyte maturation, sperm motility, and embryo developmental competence. While most data originate from in vitro bovine studies, in vivo research in sheep offers valuable insights. Importantly, given the potential for EDCs to bioaccumulate in animal tissues, these findings hold significant implications for animal health, particularly regarding reproductive physiology and fertility rates. https://doi.org/10.3390/ani15182712

Maternal Phthalate Exposure Alters Prostate Proteome in Rat Offspring: Linking Omics Insights to Prostate Cancer Risk in Humans,
Souza, P. V., Aquino, A. M., Alonso-Costa, L. G., De Oliveira, M. a. F., Rocha, V. A., Fioretto, M. N., Moreira, M. F., Pinha, V. C., Caxali, G. H., Justulin, L. A., Flaws, J. A. and Scarano, W. R., *Archives of Medical Research*, Feb 2026, Vol. 57, no. 2.

Background. Phthalates are compounds used as plasticizers to increase the flexibility of plastics and are considered endocrine disruptors. Some studies suggest that the origin of prostate cancer (PCa) may be associated with disturbances during embryo-fetal development. Previous data showed that perinatal exposure to the same phthalate mixture (PM) used here increased the incidence of adenocarcinomas in the prostates of aged rats. Building on our earlier work, this study identifies proteins altered in the prostate proteome by exposure to a PM during gestation and lactation in rats, focusing on proteins in the human secretome and their correlation with PCa. Methods. Pregnant SD rats were divided into three groups and treated from gestational day (GD)10 to postnatal day (PND)21. On PND22 the differentially abundant proteins in the offspring's prostate were compared with the predicted secreted proteins in humans. Then, the abundance of selected proteins was compared among groups and enriched. Finally, a protein-protein interaction network was obtained. The resulting data were cross-referenced with data for PCa and some targets were validated by RT-qPCR and Western blot. Results. Perinatal exposure to PM affected the endoplasmic reticulum, decreasing the amount of certain proteins crucial for protein folding and secretion, impairing secretion of several proteins important for proper prostate development. Furthermore, in silico analysis revealed that several proteins in the rat proteome are also altered in patients with PCa. Conclusions. Our results suggest that early exposure to phthalates may modulate protein secretion, creating a microenvironment that impairs tissue development and increases susceptibility to oncogenesis. (c) 2025 Instituto Mexicano del Seguro Social (IMSS). Published by Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies. https://doi.org/10.1016/j.arcmed.2025.103297

The effect of maternal sodium ρ-perfluorous nonenoxybenzene sulfonate exposure on the gut microbiota in dams and offspring,
Wang, C. Y., Ping, F. F., Tong, Q., Li, Y. Y. and Jin, Y. X., *Scientific Reports*, Aug 25 2025, Vol. 15, no. 1.

Sodium rho-perfluorous nonenoxybenzene sulfonate (OBS) is increasingly used as an effective perfluoroalkyl/polyfluoroalkyl substances (PFASs) alternative across multiple industries. This study involves exposing pregnant C57BL/6 mice to OBS at concentrations of 0, 0.5, and 5.0 mg/L via

drinking water during gestation and lactation. The investigation focused on analyzing gut microbiota in both dams and offspring after maternal OBS exposure. Results highlighted notable changes in the gut microbiota composition within the colonic content of both dams and offspring, the Bacteroidetes, Firmicutes, alpha-Proteobacteria and beta-Proteobacteria decreased significantly in dams. After maternal OBS exposure, Actinobacteria increased in F1-20 d male mice, while alpha-Proteobacteria decreased; Bacteroidetes increased, and Firmicutes and alpha-Proteobacteria decreased in F1-20 d female mice. In F1-8 w mice, Firmicutes increased and beta-Proteobacteria decreased in male, while Bacteroidetes and beta-Proteobacteria decreased in female. High-throughput sequencing confirmed that sodium rho-perfluorous nonenoxybenzene sulfonate significantly altered gut microbiota patterns in both dams and offspring. Biomarkers in dams and offspring varied after maternal OBS exposure, and differences were noticeable across genders and developmental stages. In dams, the abundance of Desulfobacterota and Peptococcaceae decreased, the abundance of RF39 and Lachnospiraceae increased. Additionally, Verrucomimicrobiota, Patescibacteria, Actinobacteriota, and Cyanobacteria at the phylum level showed significant differences between dams and offspring, while Verrucomimicrobiota and Patescibacteria differed in male and female offspring. Furthermore, functional predictions indicated shifts in metabolic pathways in both generations after maternal OBS exposure. In a word, maternal OBS exposure disrupted gut microbiota and altered the metabolism processes in dams and offspring, offering insights into potential health risks associated with maternal OBS exposure.
https://doi.org/10.1038/s41598-025-15021-9

Per- and polyfluoroalkyl substances in dog blood serum levels and semen quality,
Weiss, J., Engelhardt, J., Holst, B. S., Al-Sarraj, R. and Hallberg, I., *Frontiers in Endocrinology*, Oct 1 2025, Vol. 16.

Background Growing evidence links chemical exposure to declining reproductive function in both humans and dogs. Our aim was to investigate the exposure of a wide range of per- and polyfluoroalkyl substances (PFAS) in dog serum and to investigate the association between PFAS exposure and endocrine parameters as well as semen quality. Method Semen samples (n=65) were collected from Bernese mountain dogs during 2020. Sperm motility was evaluated under a phase-contrast microscope (100x, 200x). Total sperm count was calculated using a B ürker chamber. Sperm morphology was evaluated using standard protocols in wet preparations of semen fixed in buffered formalin and stained with carbolfuchsin-eosin. Serum was analyzed using a combined targeted and suspect screening approach for quantitative analysis of 50 PFAS. Following extraction, instrumental analysis was performed using an ultra-high-performance liquid chromatograph coupled to a Q ExactiveOrbitrap mass spectrometer. PFAS concentrations were associated with semen quality and endocrine biomarkers using Least Absolute Shrinkage and Selection Operator (LASSO) regression. Results In all samples, PFOA, PFNA, PDFA, PFPeS, PFHxS and PFOS could be detected, although PFPeS levels were not above the quantification limit. The levels of the dominant congeners were on average (5th-95th percentile) PFOA 0.44 (0.05-1.3) ng/g serum, PFHxS 0.39 (0.05-0.96) ng/g serum, and PFOS 2.1 (0.35-6.4) ng/g serum. Fifteen suspect PFAS congeners were identified, where perflouro-4-ethylcyclohexanesulfonate (PFECHS), H-PFOA, H-PFNA, and H-PFDA were found in > 60% of the samples. Significant associations were found between PFBS motility (beta = 136.56, p = 0.03) and free androgen index (beta = 0,931, p=0.02). Conclusion For the first time, levels of a wide range of target and suspect PFAS are described in dog serum. PFAS levels in dog serum were similar to those in cats and humans, confirming that humans and pets, to a considerable extent, may share exposure to PFAS through the home environment. The study contributes to bridging the existing knowledge gap of exposure to endocrine disruptors and health effects in dogs, and thus to the research infrastructure bridging between species with the benefit of both humans and pets in a true One Health approach. https://doi.org/10.3389/fendo.2025.1643703