Bulletin de veille
Perturbateurs Endocriniens
N°33 - Novembre/Décembre 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

Toxic effects of chronic occupational mercury vapor exposure on female workers of childbearing age.

Pan Y, Qu K, Li H, Song Y. *J Occup Med Toxicol*. 2025 Feb 10;20(1):5.

BACKGROUND: Few studies have been conducted on women of childbearing age with chronic mercury poisoning caused by mercury vapor exposure. METHODS: Occupational exposure, clinical symptoms and signs, laboratory tests, auxiliary examinations, treatment, and follow-up of 31 female workers with chronic mercury poisoning from a mercury thermometer processing factory who received inpatient treatment at our hospital between September 2021 and August 2022 were analyzed. RESULTS: In 31 female workers of childbearing age (23-43 years) who were chronically exposed to mercury vapor (3-31 months), urinary mercury levels exceeded the normal range. The clinical manifestations were primarily neurological (96.77%). Renal pathology of the two female workers suggested membranous nephropathy in the first stage. Some female workers experienced menstrual

abnormalities, anxiety, depression, and sleep disorders. Treatment was mainly chelation therapy supplemented with antioxidants and other symptomatic supportive treatments. All patients achieved good results after discontinuing exposure to mercury vapor and receiving treatment. However, follow-up after discharge revealed that some female workers still had insomnia. CONCLUSIONS: Occupational mercury vapor exposure is hazardous to female workers of childbearing age and increases the risk of adverse effects on their reproductive health. Occupational protection and prevention of mercury exposure in female workers of reproductive age must be emphasized.

Lien vers l'article

Associations between cadmium and lead exposure and thyroid disorders: A systematic review and meta-analysis.

Abdelgawwad El-Sehrawy AAM, Hsu CY, Saleh EAM, Moharam MM, Rekha MM, Kundlas M, et al. *J Trace Elem Med Biol*. 2025 Dec;92:127781.

Exposure to heavy metals, specifically Cadmium and lead, poses considerable public health risks, as these substances are known endocrine disruptors that can negatively influence the regulation of thyroid hormones. This systematic review and meta-analysis examine the associations between cadmium and lead exposure and thyroid disorders, including hypothyroidism, hyperthyroidism, and thyroid cancer. The study was conducted by searching PubMed, Scopus, Embase, Web of Science, and Google Scholar, identifying 23,333 studies. After removing duplicates, 4980 were excluded for reasons such as being reviews, non-English, or unrelated, and after assessing full-text, 21 studies were included for qualitative and quantitative analysis. A random-effects meta-analysis was conducted to estimate pooled odds ratios (95 % CI) for the association between heavy metal exposure and thyroid disorders, with heterogeneity assessed via the I^2 statistic. Meta-analysis confirmed significant associations between both metals and thyroid disorders. Lead exposure showed a strong relationship (pooled OR ≈ 2.7), while cadmium also demonstrated a meaningful association (pooled OR ≈ 1.6), though with moderate heterogeneity across studies, suggesting variations due to study design, exposure assessment, or demographic factors. These findings emphasize the public health importance of reducing exposure, as both metals possess endocrine-disrupting potential. Mechanistically, cadmium appears to act through oxidative and hormonal pathways, whereas lead shows stronger associations with thyroid cancer and autoimmunity, particularly in occupational settings. Limited evidence further indicates possible sex-related and gene-environment interactions. The evidence reviewed indicates that cadmium and lead may contribute to the development of thyroid disorders through various biological pathways.

Lien vers l'article

Prospective study of oil spill cleanup-related exposure to volatile organic compounds and glycemic dysregulation.

Jardel HV, Keil AP, Martin CL, Richardson DB, Stenzel MR, Stewart PA, et al. *Environ Health*. 2025 Sep 26;24(1):67.

BACKGROUND: Exposures to volatile organic compounds could influence glycemic regulation. This study examines hemoglobin A1c (HbA1c) in a cohort of oil spill cleanup workers up to 6 years post-exposure in relation to benzene, toluene, ethylbenzene, and xylenes (BTEX) exposures, individually and as a mixture, as well as a separate estimation of the aggregate sum of BTEX (total BTEX). METHODS: Data for this analysis are from the Gulf Long-term Follow-up (GuLF) Study– a prospective cohort of workers involved in the 2010 Deepwater Horizon oil spill cleanup. HbA1c and medication

information were obtained at Home Visit and Clinical Exam phases 1–3 years and up to 6 years post-exposure, respectively. Cumulative inhalation exposure to the individual BTEX chemicals and to total BTEX were estimated using a job-exposure matrix linking air measurements to detailed individual worker cleanup work histories. We used Tobit regression models to examine associations between exposure to the chemicals and latent, untreated HbA1c, accounting for medication-reduced HbA1c. We used quantile g-computation to examine exposure to the mixture of BTEX chemicals and HbA1c. RESULTS: In results examining Home Visit HbA1c we observed no discernable patterns but found suggestive evidence of an association with total BTEX. In results for Clinical Exam HbA1c, we did not observe monotonic patterns, but rather an inverted-U pattern with elevations in Q2 or Q3 or no clear pattern. Similarly, in results for final HbA1c adjusting for initial HbA1c, total BTEX difference estimates showed an inverted-U pattern in point estimates across Q2 (0.24 95%CI (0.14, 0.34)), Q3 (0.13 95%CI (0.03, 0.24)), and Q4 (0.00 95% CI (-0.11, 0.10)), compared to Q1. CONCLUSION: Exposures to the moderate levels of the BTEX chemicals observed in this study population, individually and as an aggregate, may be associated with elevated HbA1c up to 6 years after exposure, with an inverted-U pattern. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s12940-025-01211-5.

Lien vers l'article

Herbicide-related health risks: key mechanisms and a guide to mitigation strategies.

Hongoeb J, Tantimongcolwat T, Ayimbila F, Ruankham W, Phopin K. *J Occup Med Toxicol*. 2025 Feb 25;20(1):6.

BACKGROUND: Herbicides are a group of substances used to control undesired vegetation in both agricultural and non-agricultural settings. They are recorded as the most consumed class among other pesticides, reaching nearly two million tons worldwide. Despite their effectiveness in weed control, the extensive utilization of herbicides has raised concerns regarding adverse effects on human health. However, comprehensive reviews addressing herbicide-related human health risks remain limited. This work aims to compile scientific evidence and possible underlying mechanisms to emphasize the hazards that need to be acknowledged, as well as to explore novel strategies for minimizing the impact on human health. METHOD: Scientific data on herbicide-related human health risks, including human-related data and non-human experimental research, were retrieved from databases such as PubMed, Scopus, and Google Scholar. Pre-determined eligibility criteria were applied to select the final studies. RESULT: A narrative summary of evidence-based human incidence and laboratory experiments is presented to organize and highlight key findings. This indicates the life-threatening nature of herbicide exposure in humans, ranging from acute toxicity to the development of chronic diseases at any stage of life. CONCLUSION: Herbicidal chemicals can harm individuals through various pathways, especially by inducing oxidative stress or directly disrupting molecular and cellular processes. Despite some conflicting findings, effective mitigation strategies are urgently needed to promote a safer society and protect human well-being.

Lien vers l'article

Risk of longer-term endocrine and metabolic conditions in the Deepwater Horizon Oil Spill Coast Guard cohort study - five years of follow-up.

Denic-Roberts H, Engel LS, Buchanich JM, Miller RG, Talbott EO, Thomas DL, et al. *Environ Health*. 2025 Mar 22;24(1):12.

INTRODUCTION: Long-term endocrine and metabolic health risks associated with oil spill cleanup exposures are largely unknown, despite the endocrine-disrupting potential of crude oil and oil dispersant constituents. We aimed to investigate risks of longer-term endocrine and metabolic conditions among U.S. Coast Guard (USCG) responders to the Deepwater Horizon (DWH) oil spill. METHODS: Our study population included all active duty DWH Oil Spill Coast Guard Cohort members (N = 45,224). Self-reported spill exposures were ascertained from post-deployment surveys. Incident endocrine and metabolic outcomes were defined using International Classification of Diseases (9th Revision) diagnostic codes from military health encounter records up to 5.5 years post-DWH. Using Cox proportional hazards regression, we estimated adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) for various incident endocrine and metabolic diagnoses (2010-2015, and separately during 2010-2012 and 2013-2015). RESULTS: The mean baseline age was 30 years (~ 77% white, ~ 86% male). Compared to non-responders (n = 39,260), spill responders (n = 5,964) had elevated risks for simple and unspecified goiter (aHR = 2.09, 95% CI: 1.29-3.38) and disorders of lipid metabolism (aHR = 1.09, 95% CI: 1.00-1.18), including its subcategory other and unspecified hyperlipidemia (aHR = 1.10, 95% CI: 1.01-1.21). The dysmetabolic syndrome X risk was elevated only during 2010-2012 (aHR = 2.07, 95% CI: 1.22-3.51). Responders reporting ever (n = 1,068) vs. never (n = 2,424) crude oil inhalation exposure had elevated risks for disorders of lipid metabolism (aHR = 1.24, 95% CI: 1.00-1.53), including its subcategory pure hypercholesterolemia (aHR = 1.71, 95% CI: 1.08-2.72), the overweight, obesity and other hyperalimentation subcategory of unspecified obesity (aHR = 1.52, 95% CI: 1.09-2.13), and abnormal weight gain (aHR = 2.60, 95% CI: 1.04-6.55). Risk estimates for endocrine/metabolic conditions were generally stronger among responders reporting exposure to both crude oil and dispersants (vs. neither) than among responders reporting only oil exposure (vs. neither). CONCLUSION: In this large cohort of active duty USCG responders to the DWH disaster, oil spill cleanup exposures were associated with elevated risks for longer-term endocrine and metabolic conditions.

Lien vers l'article

Firefighting, other protective service occupations and prostate cancer risk: a pooled analysis of three case-control studies.

Bijoux W, Parent M, Richard H, Castaño-Vinyals G, Pollán M, Kogevinas M, et al. *J Occup Med Toxicol*. 2025 Jun 10;20(1):20.

BACKGROUND: Prostate cancer (PCa) is the most frequent incident cancer among males in industrialized countries, but little is known about its aetiology. A role for occupational exposures is suggested. Occupational exposure as a firefighter, a protective service occupation (PSO), is classified as carcinogenic to humans by the International Agency for Research on Cancer, with limited evidence in humans for PCa. We studied the association between PSO and PCa risk considering tumour aggressiveness and screening practices. METHODS: The EPIdemiological study of Prostate Cancer (EPICAP), the Prostate cancer & Environment Study (PROtEuS) and the MultiCase-Control study in common tumours in Spain (MCC-Spain) are population-based case-control studies, conducted respectively in France, Canada, Spain, in 2005–2014 in men ≤ 85 years old, including overall 3,859 incident cases and 4,359 controls frequency-matched on age. Participants were interviewed face-to-face using general and occupational questionnaires covering all jobs held in career, coded according to the 1988 International Standard Classification of Occupations. Unconditional logistic regressions estimated associations between PSO and PCa, after adjusting for potential confounders. Two sets of analyses were conducted, without and with consideration of screening. The latter is believed to yield the main findings since less subject to detection bias. RESULTS: When restricting controls to those recently screened, men employed as firefighters ≥ 10 years had increased risk (OR (Odds ratio) = 2.01

[95% confidence interval] [1.02; 3.97]) of non-aggressive PCa. Positive associations for non-aggressive PCa among men employed < 10 years as police officers (OR = 2.53 [1.07; 5.96]) and police inspectors and detectives (OR = 6.75 [1.47; 30.96]) were observed. Very few cases in PSO were characterized by aggressive tumours. CONCLUSIONS: Findings from this large population-based study corroborate the higher PCa risk previously reported among firefighters, but only for non-aggressive tumours. Screening practices had a substantial impact on risk estimates. Future studies should investigate specific exposures, and account for PCa aggressiveness and individual screening patterns. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1186/s12995-025-00464-7.

Lien vers l'article

Lead exposure is associated with increased lead bioaccumulation and a decline in semen quality: a systematic review and meta-analysis.

Adisa VI, Ashonibare PJ, Adegbola CA, Akhigbe TM, Kolawole OR, Omole IA, et al. *JBRA Assist Reprod*. 2025 Dec 10;29(4):764-82.

OBJECTIVE: This systematic review and meta-analysis aimed to assess the impact and associated mechanisms of lead on human semen quality. METHODS: A systematic search was conducted from March 18th to April 30th, 2024, utilizing Google Scholar, PubMed, and Scopus, and applying the PECOS model to identify relevant studies. RESULTS: A total of seventeen studies fulfilled the inclusion criteria. The results of our analysis indicated that blood lead levels were markedly elevated in men exposed to lead compared to control subjects (SMD -7.06 [95% CI: -9.03, -5.08], p<0.00001), with analogous results observed for semen lead levels (SMD -3.42 [95% CI: -5.22, -1.62], p=0.0002). Lead exposure was linked to significant decreases in ejaculate volume (SMD 0.81 [95% CI: 0.16, 1.45], p=0.02), sperm count (SMD 2.10 [95% CI: 1.11, 3.09], p<0.0001), sperm concentration (SMD 0.77 [95% CI: 0.09, 1.44], p=0.03), and total motility (SMD 2.20 [95% CI: 1.28, 3.11], p<0.00001), as well as an increase in abnormal sperm morphology (SMD -3.29 [95% CI: -4.87, -1.71], p<0.0001). While reductions in testosterone levels and elevations in semen malondialdehyde were noted, these changes did not reach statistical significance. CONCLUSIONS: This study demonstrates that lead exposure is associated with reduced sperm quality. The present findings highlight the urgent need for strategies to reduce lead exposure and emphasize the importance of further research into potential mitigating interventions.

Lien vers l'article

Thyroid Function Effects of Mixed Exposure to Urinary Trihalomethanes and Haloacetic Acids: Based on an Integrated Framework of Exposure Assessment, Qualitative Association, and Quantitative Attribution,
Bai, X., Du, Z. Y., Wu, Y. T., Qian, J. F., Gu, T. M., Liu, S. L., Men, H., Wu, Y., Xiong, J. S., Sun, K., Liu, L. X., Shi, Y. W. and Zheng, W. W., *Environmental Science & Technology*, 2025.

Toxicological studies have demonstrated that disinfection byproducts (DBPs) can disrupt thyroid function; however, human epidemiological evidence remains limited. The existing studies focus on a limited number of compounds and lack detailed investigation of mixed exposure effects. To address these gaps, we developed a three-tier analytical approach that includes exposure assessment, qualitative association, and quantitative attribution. A total of 435 community-dwelling adults in Shanghai, China, were enrolled, and urinary concentrations of 16 DBPs, including halomethanes

(HMs) and haloacetic acids (HAAs), and five serum thyroid function indicators were measured. We detected HAAs at higher concentrations than HMs and chlorinated DBPs, generally exceeding brominated and iodinated species. Key DBP exposure risk factors include age, occupation, education, indoor time, occupational water contact, income, body mass index, and sex. Both individual and mixture-based DBP exposures were significantly associated with thyroid hormone indicators (triiodothyronine and free thyroxine) and immune-related markers (thyroglobulin antibody and thyroid peroxidase antibody). HAAs contributed more to thyroid disruption, with trichloroacetic acid identified as a compound of particular concern. This study offers the first systematic assessment of HAA and HM mixture effects on thyroid function indicators and provides an analytical framework for evaluating the health impacts of pollutant mixture exposures. https://doi.org/10.1021/acs.est.5c10266

Cadmium toxicity-related metabolic bone disease: a clinical conundrum of five cases, Giri, S., Roy, A., Kumar, A., Ghosh, S., Bhunia, A. and Patra, S., *Osteoporosis International*, 2025.

Cadmium exposure from jewellery-making fumes can damage bones and kidneys. In five goldsmiths, we found osteoporosis, fractures, and renal dysfunction linked to high cadmium levels. Both direct toxicity and indirect effects through kidney damage and hormones contributed. Awareness and early detection may prevent irreversible complications.IntroductionCadmium (Cd) is a highly toxic heavy metal with established skeletal and renal toxicity. Inhalation of Cd fumes during jewellery-making is an underrecognized occupational hazard in India. We report five goldsmiths with chronic Cd exposure who developed varying patterns of metabolic bone disease, aiming to highlight the diverse mechanisms of Cd-induced osteopathy.MethodsFive patients with occupational exposure to Cd in jewellery-making were evaluated through detailed clinical history, biochemical investigations (renal and metabolic profile, bone turnover markers, intact fibroblast growth factor 23 levels), dual-energy X-ray absorptiometry (DXA), and Cd measurement by inductively coupled plasma mass spectrometry. Renal tubular function was assessed with urinary beta 2-microglobulin and serum uric acid.ResultsAll five patients exhibited skeletal involvement, ranging from osteopenia to severe osteoporosis and fractures. Case 1 had proximal renal tubular acidosis, hypophosphatemic osteomalacia, secondary hyperparathyroidism, and progressive cortical bone loss, with clinical improvement after supplementation therapy. Case 2 showed proximal myopathy, osteoporosis, and cardiomyopathy, with renal phosphaturia. Cases 3-5 demonstrated primarily cancellous bone loss with variable renal tubular dysfunction and markedly elevated Cd levels. Hypophosphatemia was mediated by both tubular damage and FGF23-dependent mechanisms. Hypouricemia emerged as a sensitive biomarker of early tubular injury.ConclusionsChronic occupational Cd exposure in goldsmiths causes diverse skeletal manifestations through direct osteotoxicity, hypophosphatemia from renal tubular dysfunction and FGF23 excess, and secondary hyperparathyroidism. The toxic effect preferentially involves cancellous bone, while renal-mediated mechanisms contribute to cortical bone loss. Early recognition via occupational history, supported by simple biomarkers such as serum uric acid, is essential to prevent irreversible complications. Supplementation with calcium, phosphate, vitamin D analogues, and supportive therapy can stabilize bone health and improve outcomes. https://doi.org/10.1007/s00198-025-07810-9

Association between hair dye use and human cancers: A systematic review, Greene, R. K., Maghfour, J., Nguyen, C., Baker, G. and Mesinkovska, N. A., *Jaad International*, Feb 2026, Vol. 24, p. 205-233.

Background: The global hair color market is valued over 23 billion dollars with over 2 billion in sales in the United States. Permanent hair dye accounts for approximately 80% of hair dye products on the market. Objective: To systematically review the association between hair dye use and cancer

risk and identify vulnerable populations. Methods: A systematic search of PubMed and MEDLINE from January 1964 to March 2025 was conducted. Articles were reviewed independently by 3 assessors. Results: The review included 96 articles including 2 on both adults and children, and 5 on maternal exposure and pediatric cancer risk. Some studies suggested potential associations between hair dye use and cancer risk. Trends include increased risk of estrogen receptor 1 breast cancer among African American women and elevated bladder cancer in both genders. risk in frequent users. Individuals with slow acetylator N-acetyltransferase 2 genotypes or CYP1A2 had elevated cancer risk with dye use. Maternal use during the first trimester significantly increased offspring risk of acute lymphoblastic leukemia further elevated by continued use during lactation. Limitations: Limitations include elements of study design, study populations, and confounders. Conclusion: There is evidence to suggest possible increased cancer risks for frequent, long-term hair dye use in specific populations. https://doi.org/10.1016/j.jdin.2025.10.009

Heavy metals and human reproductive toxicity: Mechanisms, pregnancy outcomes, and mitigation strategies,
Marconi, G., Di Resta, C., Naclerio, A., Banfi, G. and Tomaiuolo, R., *Reproductive Toxicology*, Jan 2026, Vol. 139.

Heavy metals are environmental pollutants with well-documented systemic toxicity. Emerging evidence highlights their detrimental effects on human reproductive health. This narrative review aims to synthesize current scientific literature on the reproductive toxicity of arsenic (As), cadmium (Cd), chromium (Cr), mercury (Hg), and lead (Pb), focusing on their impact on fertility, pregnancy outcomes, fetal development, and neonatal health. The analysis includes cellular, molecular, and endocrine mechanisms, and considers both chronic environmental and acute occupational exposures. Inclusion criteria comprised peer-reviewed experimental, clinical, and review studies involving human subjects, providing direct translational relevance. Key endpoints included gametogenesis, hormonal regulation, fertility outcomes, and pregnancy complications. The main mechanisms of heavy metal-induced reproductive toxicity include DNA damage, oxidative stress, apoptosis, ionic mimicry, and hormonal disruption. In males, exposure is associated with reduced sperm quality, altered morphology, and impaired motility. In females, heavy metals interfere with oocyte maturation, ovarian function, and hormonal balance, increasing the risk of infertility, miscarriage, and adverse pregnancy outcomes. In addition to summarizing toxic effects, the review also discusses emerging protective and mitigation strategies-such as micronutrient and antioxidant supplementation-that may counteract reproductive damage. Heavy metal exposure, even at low levels, poses a significant risk to human reproductive health. The findings underscore the urgent need for preventive strategies, environmental regulation, and targeted health monitoring, particularly among vulnerable populations. Future research should explore the long-term and transgenerational effects of exposure. https://doi.org/10.1016/j.reprotox.2025.109104

Assessment of sex hormones in operating room personnel exposed to a mixture of waste anesthetic gases,
Neghab, M. and Amiri, F., *Annals of Work Exposures and Health*, Nov 2025, Vol. 69, no. 9, p. 951-958.

The balance of male and female sex hormones is essential for maintaining and regulating the reproductive process. This retrospective cohort study aimed to assess the relationship between long-term occupational exposures to waste anesthetic gases (WAGs), comprising a mixture of sevoflurane, isoflurane, and nitrous oxide (N2O), and the levels of sex hormones in operating room personnel. The sample included 39 operating room staff who had been exposed to WAGs for more than 1 year without any pre-existing medical conditions or diseases that could affect the

reproductive system, and 37 healthy employees from other hospital wards who had no occupational exposure to WAGs. Blood samples were collected from the antecubital vein on days 2 to 3 of the menstrual cycle of female subjects for measurement of luteinizing hormone, follicle-stimulating hormone (FSH), and anti-M & uuml;llerian hormone. Furthermore, serum levels of luteinizing hormone, FSH, testosterone, and inhibin B were measured in male individuals by the ELISA method. Among exposed participants, the urinary concentrations of sevoflurane and N2O, but not isoflurane, were higher than the proposed biological exposure values for these agents. The serum levels of sex hormones in WAGs-exposed operating room staff were significantly lower than in the unexposed participants, with Cohen's d coefficients higher than 0.8, in both sexes. After adjusting for potential confounders, significant associations were found between sex hormone levels and long-term exposure to these chemicals. The results of our study indicated that chronic occupational exposure to high levels of WAGs, especially N2O, is related to damage to the expression and metabolism of sex hormones. The prolonged effects of these impacts on the function of female and male reproductive systems require further investigation. https://doi.org/10.1093/annweh/wxaf072

Hormonal changes in professional printers exposed to phthalates suggesting potential disturbances of the hypothalamic-pituitary-gonadal axis,
Nita, T. M., Wrobel, S. A., Vernez, D., Koch, H. M., Wild, P., Zufferey, F., Rudaz, S., Stenz, L., Odermatt, A. and Hopf, N. B., *Environmental Research*, Feb 15 2026, Vol. 291.

Background: Phthalate exposures might alter male reproductive health, but human evidence remains limited and inconsistent. Occupational settings often involve consistently high exposures from known sources, providing a basis for developing risk reduction strategies and interventions. Objectives: Evaluate dose-response relationships between phthalate exposures in professional printers (urinary metabolites) and male reproductive hormones, which were examined twice in one working week for workweek values (mean) and within-week changes, (ratio) responses. Methods: Occupational biomonitoring of 59 male printers was used to assess exposures to 18 phthalates by measuring 35 urinary phthalate metabolites. Blood samples collected on the first and last day of the workweek were analyzed for total testosterone, calculated free testosterone (cFT), bioavailable testosterone (BioT), measured free testosterone, sex hormone-binding globulin (SHBG), luteinizing hormone, follicle-stimulating hormone, prolactin, estradiol (E2), and inhibin B (INHB). Multiple covariate-adjusted linear regressions were used to evaluate the dose-response relationship. Results: cFT hormonal workweek response was negatively associated with di-n-butyl phthalate (DnBP) metabolites while SHBG was positively associated with diethyl-hexyl phthalate (DEHP) metabolites. BioT and E2 within-week responses were negatively associated with the DiBP metabolite mono-2-hydroxy-isobutyl phthalate (2OH-MiBP). Overall, ten low-molecular-weight phthalate metabolite concentrations were positively associated with INHB, while eight high-molecular-weight phthalate metabolite concentrations were negatively associated with FSH. Occupational exposure to these phthalates was elevated, as median concentrations of their metabolites were between 2-to 7-fold higher than general population levels. Conclusions: Occupational exposures to certain phthalates in professional printers were associated with hormonal patterns, indicative of anti-androgenic reproductive disturbance and potential alteration of the HPG axis.
https://doi.org/10.1016/j.envres.2025.123477

Association of oil spill cleanup-related hydrocarbon exposure with incident hypertension up to 11 years after exposure in the Gulf Long-term Follow-up Study,
Patel, O. P., Edwards, J. K., Kucharska-Newton, A. M., Whitsel, E. A., Christenbury, K. E., Jackson Ii, W. B., Lawrence, K. G., Stewart, P. A., Stenzel, M. R., Engel, L. S. and Sandler, D. P., *Environ Health*, Dec 30 2025.

BACKGROUND: While several studies have found positive associations between exposure to oil spill cleanup-related chemicals and hypertension, no study has examined these associations longitudinally. OBJECTIVE: This study examined associations of oil spill-related benzene, toluene, ethylbenzene, xylene, and n-hexane (BTEX-H) exposures, individually and as both the aggregate sum (total) of BTEX-H and the BTEX-H mixture with incident hypertension among Gulf Long-term Follow-up (GuLF) Study participants. METHODS: Participants were 18,619 Deepwater Horizon (DWH) oil spill cleanup and response workers who enrolled in the GuLF Study (2011-2013). Cumulative exposures to each BTEX-H chemical were estimated with a job-exposure matrix linking detailed self-reported DWH participant work histories to exposure group estimates developed from air monitoring data. We defined incident hypertension as the first self-reported physician diagnosis of hypertension or high blood pressure after each worker's last date of cleanup work, as reported at enrollment or a follow-up interview (2013-2016 or 2017-2021). We used Cox proportional hazards regression to estimate hazard ratios (HR) and 95% confidence intervals (CI). We used quantile g-computation to estimate the joint effect of the BTEX-H mixture. RESULTS: Approximately 20% (n = 3,779) of workers reported an incident hypertension diagnosis. Exposures to the individual BTEX-H chemicals were highly correlated (r = 0.87-0.95). The HRs comparing the highest to lowest quartiles of individual BTEX-H and total BTEX-H exposures ranged from 1.27 to 1.35. We found evidence of exposure-response trends across increasing quartiles of exposure. Each one quartile increase in the BTEX-H mixture was positively associated with incident hypertension (HR: 1.10, 95% CI: 1.07, 1.14). DISCUSSION: Oil spill cleanup work-related BTEX-H exposures were associated with the risk of incident hypertension, extending prior findings of cross-sectional associations. Since BTEX-H exposures are common in occupational and population settings, these findings may have broader public health implications. https://doi.org/10.1186/s12940-025-01253-9

Polybrominated Diphenyl Ethers, Occupational Exposures, and Thyroid Function Among US and Canadian Firefighters,
Rothberg, B. E. G., Caban-Martinez, A. J., Barr, D. B., Jara, M. A., Rodriguez, V., Feliciano, P. L., Santiago, K. M., Beaver, C. C., Kobetz-Kerman, E. N. and Solle, N. S., *Journal of Occupational and Environmental Medicine*, Nov 2025, Vol. 67, no. 11, p. 935-942.

Objective Evaluate the association between serum polybrominated diphenyl ether (PBDE) levels and thyroid anatomy and function in firefighters. Methods Two hundred fifty-nine firefighters provided a blood sample and underwent thyroid ultrasound. Blood serum levels were tested for thyroid function tests and PBDEs -47, -85, -99, -100, -153, and -154 (ng/g lipid weight). Ultrasonography documented structural characteristics. Bivariate associations between PBDE concentrations and demographic/occupational characteristics, thyroid function, and thyroid anatomic measures were determined using multivariable linear regression. Results A positive relationship between PBDE-47 and triiodothyronine (P = 0.02) while an inverse relationship with free thyroxine (P = 0.03) was observed. PBDE-47 was inversely associated with thyroid nodule size (P = 0.03) and nodule aggressiveness (P = 0.02). PBDE-47 was highest in western United States firefighters and lowest among sampled Canadians (P = 0.01). Conclusions PBDE-47 may contribute to thyroid dysregulation in firefighters. PBDE-47 levels differ across North America.
https://doi.org/10.1097/jom.0000000000003477

Microplastics toxicity: Classification, sources, exposure routes, and experiments,
Salih, W. Y., Hassan, F. M. and Sabbah, M. A., *Desalination and Water Treatment*, Jan 2026, Vol. 325.

Microplastics (MPs), including polymers such as polyethylene, polyvinyl chloride (PVC), and polystyrene (PS), are widespread environmental contaminants detected in air, water, soil, and food.

These particles originate from the breakdown of larger plastics and from direct industrial and consumer sources, including packaging, textiles, and personal care products. MPs enter the human body primarily through ingestion, inhalation, and dermal contact, with food, water, and air serving as major exposure pathways. Once internalized, MPs have been found in various human tissues and biological fluids, indicating their capacity for bioaccumulation. Toxicological studies in experimental models and occupational settings link MP exposure to oxidative stress, inflammation, cellular dysfunction, and potential organ toxicity, including effects on the gastrointestinal, respiratory, immune, reproductive, and nervous systems. PVC microplastics, in particular, are associated with liver toxicity and increased cancer risk in occupationally exposed populations. MPs can also act as vectors for environmental pollutants and plastic-associated chemicals, further amplifying health risks. This review summarizes the classification, major sources, exposure routes, and toxicological activity of MPs. A comprehensive understanding of MP properties is essential for developing effective strategies to mitigate their persistent harmful effects on public health and the environment. https://doi.org/10.1016/j.dwt.2025.101599

Prevalence of Toxic Exposures Among Women Veterans With Breast or Gynecologic Cancers Receiving Veterans Affairs (VA) Care,
Shepherd-Banigan, M., Cummin, G. L., Berkowitz, T. S., Weidenbacher, H. J., Moss, H., Chawla, N., Goldstein, K. M., Hazra, A., Bayley, E. M., Colonna, S., Smith, I., Halwani, A. S., Kelley, M. J. and Zullig, L. L., *Military Medicine*, 2025.

Introduction Toxic exposures have been linked to hormonal disruption and DNA damage, increasing risk for hormone-sensitive cancers, such as breast and gynecologic cancers. However, the effect of toxic exposure on women Veteran cancer risk is unknown, especially for Veterans who served in the recent Middle East conflict because of the latency with which cancer develops. This study assesses the prevalence of toxic exposures among women Veterans with diagnosed breast and gynecologic cancers.Materials and Methods This descriptive, cross-sectional study examines self-reported toxic exposures among Veterans diagnosed with breast or gynecologic cancers in the Veterans Health Administration and who participated in a clinical care survey with a nurse navigator. Data were obtained from Veteran Health Affairs (VA) electronic medical records and data from the Breast and Gynecologic Oncology System of Excellence (BGSoE) Program Dashboard. Exposure categories include air pollutants, occupational hazards, chemicals, physical agents, and biological risks. We compared demographic, health, and geographic factors between Veterans who reported hazardous exposure versus those who did not and described the characteristics of those hazards.Results Nearly 50% of women Veterans in the sample reported experiencing a hazardous exposure during military service. Over 80% reported feeling very or somewhat concerned about the exposure. Airborne exposures were the most frequently reported.Conclusions Women Veterans with breast and/or gynecologic cancer frequently report hazardous exposures during military service, which may impact their actual and perceived cancer risk and subsequent health care utilization. Future research is needed to assess the relationship between perceived/reported and actual hazardous exposures and inform any needed cancer interception. https://doi.org/10.1093/milmed/usaf561

Occupational exposure to phthalate esters and systemic clinical changes in municipal sanitation workers: Human biomonitoring and network analysis approach,
Tangestani, M., Yazdi, N. B., Arfaeinia, H., Soleimani, F., Zanganeh, Z., Afrashteh, S., Farhadi, A., Moftian, N., Mansouri, M. and Zare, S., *Environmental Pollution*, Feb 1 2026, Vol. 390.

Continuous exposure to products containing phthalate acid esters (PAEs) has generated concerns regarding their impact on human health. This study was aimed at evaluating occupational exposure to PAEs metabolites among 90 municipal waste collection workers compared to 90 staff involved in

janitorial duties across academic, administrative, and institutional areas (as a control group). Blood serum samples were analyzed to quantify multiple PAEs metabolites, alongside assessments of hematological, biochemical, inflammatory, oxidative stress, liver, thyroid, and kidney function biomarkers. Results showed significantly higher PAEs metabolite levels in exposed workers (total PAEs mean +/- standard deviation: 25.66 +/- 12.81 mu g/L vs. 15.03 +/- 5.14 mu g/L, p < 0.001), accompanied by alterations in blood indices-including decreased white blood cells (WBC) and hemoglobin (HB), elevated red blood cells (RBC) and eosinophils-and elevated liver enzymes, thyroid hormones, and inflammatory markers such as the inflammatory cytokines tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6). The findings suggest that PAEs' metabolite levels are largely unaffected by demographic and lifestyle factors, highlighting occupational exposure as the predominant source in this group. Network analysis revealed that occupational exposure to PAEs, including Mono(2-ethylhexyl) phthalate (MEHP), in municipal sanitation workers is associated with significant alterations in neutrophils, 8-hydroxy-2 '-deoxyguanosine, (OHdG8), thyroid parameters (triiodothyronine (T3) and thyroxine (T4), prothrombin time)PT(.), and hematological factors (albumin, mean corpuscular hemoglobin concentration)MCHC(.), and partial thromboplastin time (PTT)). These findings highlight the impact of occupational PAEs exposure on multiple physiological systems and underscore the need for preventive measures and continuous health monitoring in this population. https://doi.org/10.1016/j.envpol.2025.127494

Assessment of early kidney function biomarkers and environmental exposure to contaminant mixtures in Mexican brick-making workers under precarious labor conditions,
Axel, R. Z., Javier, P. F., Juan-Carlos, F. M., Olivier, B., Manolo, O. R., Kelvin, S. V. and Beatriz, M. K., *Environ Toxicol Pharmacol*, Jan 2026, Vol. 121, p. 104893.

Artisanal brick-making exposes workers to mixtures of environmental contaminants under precarious conditions. This study assessed exposure to PAHs, arsenic, fluoride, lead, and their associations with early kidney damage biomarkers in 109 adults from three brick-making communities in central Mexico. Urinary and blood concentrations of contaminants were measured using validated analytical methods, and renal biomarkers (CYS-C, B2M, OPN, KIM-1, NGAL) were quantified via multiplex ELISA. Median urinary concentrations of 1-OH-PYR (1.3-2.3 µmol/mol uCr), arsenic (20.8-45.3 µg/L), and fluoride (1.6-2.6 mg/g uCr) exceeded reference values in a substantial proportion of participants. Cystatin-C and osteopontin showed significant associations with arsenic, fluoride, and PAH metabolites, including nonlinear relationships. No consistent associations were found for NGAL or KIM-1. These findings provide evidence of early renal alterations related to environmental exposures and support the utility of early-effect biomarkers for public health surveillance in vulnerable populations exposed to nephrotoxic mixtures under informal occupational conditions. https://doi.org/10.1016/j.etap.2025.104893

Hormonal changes in professional printers exposed to phthalates suggesting potential disturbances of the hypothalamic-pituitary-gonadal axis,
Nita, T. M., Wrobel, S. A., Vernez, D., Koch, H. M., Wild, P., Zufferey, F., Rudaz, S., Stenz, L., Odermatt, A. and Hopf, N. B., *Environ Res*, Feb 15 2026, Vol. 291, p. 123477.

BACKGROUND: Phthalate exposures might alter male reproductive health, but human evidence remains limited and inconsistent. Occupational settings often involve consistently high exposures from known sources, providing a basis for developing risk reduction strategies and interventions. OBJECTIVES: Evaluate dose-response relationships between phthalate exposures in professional printers (urinary metabolites) and male reproductive hormones, which were examined twice in one working week for workweek values (mean) and within-week changes, (ratio) responses. METHODS: Occupational biomonitoring of 59 male printers was used to assess exposures to 18 phthalates by

measuring 35 urinary phthalate metabolites. Blood samples collected on the first and last day of the workweek were analyzed for total testosterone, calculated free testosterone (cFT), bioavailable testosterone (BioT), measured free testosterone, sex hormone-binding globulin (SHBG), luteinizing hormone, follicle-stimulating hormone, prolactin, estradiol (E2), and inhibin B (INHB). Multiple covariate-adjusted linear regressions were used to evaluate the dose-response relationship. RESULTS: cFT hormonal workweek response was negatively associated with di-n-butyl phthalate (DnBP) metabolites while SHBG was positively associated with di-ethyl-hexyl phthalate (DEHP) metabolites. BioT and E2 within-week responses were negatively associated with the DiBP metabolite mono-2-hydroxy-isobutyl phthalate (2OH-MiBP). Overall, ten low-molecular-weight phthalate metabolite concentrations were positively associated with INHB, while eight high-molecular-weight phthalate metabolite concentrations were negatively associated with FSH. Occupational exposure to these phthalates was elevated, as median concentrations of their metabolites were between 2- to 7-fold higher than general population levels. CONCLUSIONS: Occupational exposures to certain phthalates in professional printers were associated with hormonal patterns, indicative of anti-androgenic reproductive disturbance and potential alteration of the HPG axis. https://doi.org/10.1016/j.envres.2025.123477

Metal and metalloid exposure and cognitive function among copper mine workers: A three-year longitudinal study,
Soltani, N., Sadeghi, T., Saadloo, M., Baneshi, M. R., Chermahini, S. A. and Shamsizade, A., *Neurotoxicology*, Dec 2025, Vol. 111, p. 103349.

Occupational exposure to heavy metals is increasingly recognized as a threat to neurological health. This three-year longitudinal study investigated the relationship between heavy metal exposure and cognitive performance among 69 copper miners and 74 non-miner controls. Blood concentrations of heavy metals were determined using atomic absorption spectrophotometry, while cognitive performance was assessed with standardized neuropsychological tests, including the Mini-Mental State Examination (MMSE), Symbol Digit Modalities Test (SDMT), Paced Auditory Serial Addition Test (PASAT), Psychomotor Vigilance Task (PVT), creativity measures, and the Beck Depression Inventory. The results demonstrated significantly higher blood levels of arsenic and lead in miners compared with controls, whereas copper levels showed no meaningful group difference. Elevated arsenic concentrations were strongly associated with reduced performance on the oral SDMT, reflecting impairments in information processing speed and working memory. Longitudinal analyses confirmed persistent group differences in neurocognitive outcomes, with age and education exerting notable modifying effects. Interestingly, miners consistently exhibited lower depression scores across the study period, despite greater exposure to toxic metals. These findings indicate that chronic occupational exposure to arsenic and lead contributes to subtle but measurable cognitive deficits in copper miners, particularly in domains of working memory and processing speed. https://doi.org/10.1016/j.neuro.2025.103349

Epidémiologie

Effects of exposure to 17 endocrine disrupting chemicals on sex steroid hormone levels in 12-to 19-year-old males in the United States,
Adili, A., Liu, H. R., Tian, H., Ji, Y. Y. and Han, X. F., *Reproductive Toxicology*, Dec 2025, Vol. 138.

Endocrine disrupting chemicals are widespread in the environment and can interfere with reproductive hormone regulation, but their effects during adolescence are not yet clear. This study

investigated the associations between exposure to multiple endocrine disrupting chemicals and sex steroid hormone levels in adolescent males. Data were obtained from the National Health and Nutrition Examination Survey 2013-2016, including males aged 12-19 years. Urinary concentrations of 17 endocrine disrupting chemicals, including phthalates, phenols, and parabens, were analyzed in relation to serum sex hormones. Associations were examined using linear regression, quantile g-computation, and Bayesian kernel machine regression to capture both single and mixture exposures. Linear regression identified inverse associations of mono-(3-carboxypropyl) phthalate with total testosterone, estradiol, free androgen index, free testosterone, and bioavailable testosterone. Mono-(2-ethyl-5-hydroxyhexyl) phthalate was inversely associated with estradiol, free androgen index, free testosterone, and bioavailable testosterone, but positively associated with sex hormone-binding globulin. Quantile g-computation confirmed these relationships, while Bayesian kernel machine regression demonstrated that combined exposure to 17 endocrine disrupting chemicals collectively reduced total testosterone, estradiol, free androgen index, free testosterone, and bioavailable testosterone, while increasing sex hormone-binding globulin. These findings reveal a consistent pattern of elevated binding globulin levels accompanied by decreased bioactive sex hormones. In conclusion, exposure to endocrine disrupting chemicals, both individually and as mixtures, is associated with altered sex steroid hormone levels in adolescent males. These results underscore the importance of environmental regulation to limit exposure during this critical developmental stage and highlight the potential role of chemical mixtures in adolescent reproductive health. https://doi.org/10.1016/j.reprotox.2025.109078

Urinary phthalate metabolites and central precocious puberty in girls: Evidence for luteinizing hormone mediation,
Al-Saleh, I., Elkhatib, R., Alsagheir, A., Sultana, H., Alhusayn, K., Aldgither, S., Alvi, S. N., Aljerayed, Y., Baali, M. and Devol, E., *Journal of Hazardous Materials Advances*, Feb 2026, Vol. 21.

There is growing concern that endocrine-disrupting chemicals (EDCs) may contribute to the rising incidence of central precocious puberty (CPP). This case-control study examined whether urinary concentrations of phthalate metabolites and bisphenol A (BPA) are associated with CPP risk. We recruited 77 girls (20 with idiopathic CPP and 57 age-matched controls) between 2021 and 2025 from a tertiary hospital in Saudi Arabia. Urinary EDCs were quantified using ultra-performance liquid chromatography-tandem mass spectrometry, and serum reproductive hormones, including luteinizing hormone (LH), follicle-stimulating hormone, estradiol, and cortisol, were assessed. Although urinary BPA and phthalate levels did not differ significantly between groups, LH correlated positively with several DEHP metabolites among CPP cases (rs = 0.34-0.45, p < 0.05). Specifically, di(2-ethylhexyl) phthalate (DEHP)-related metabolites-mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)-were most consistently associated. Logistic regression suggested an increased risk trend for the molar sum of three DEHP metabolites (& sum;3DEHP; OR = 2.18; 95 % CI: 0.86-5.52) and the sum of high-molecular-weight (HMW) phthalates (& sum;HMW; OR = 1.91; 95 % CI: 0.77-4.78), though not statistically significant. Cortisol levels did not differ between groups, but in CPP cases, moderate positive correlations were observed with MECPP and monobenzyl phthalate. BPA showed no significant associations with reproductive hormones or cortisol. Mediation analysis indicated borderline indirect effects via LH for several DEHP metabolites (MEOHP, MEHHP) and monobutyl phthalate (MnBP). Although MnBP showed the largest effect estimate, MEOHP was the most statistically suggestive (indirect effect = 0.79, p = 0.077). In conclusion, DEHP-related phthalates may influence early pubertal development through LH-mediated pathways. This study is novel in identifying LH as a potential mediator and detecting cortisol-phthalate correlations in CPP cases, underscoring the need for larger longitudinal cohorts with repeated biomonitoring to validate these findings. https://doi.org/10.1016/j.hazadv.2025.100955

Association between exposure to selected endocrine-disrupting chemicals and subclinical carotid atherosclerosis: A systematic review and meta-analysis,
Assempoor, R., Abroy, A. S. and Yunesian, M., *Environmental Research*, Jan 1 2026, Vol. 288.

Background: Atherosclerosis is a leading cause of death worldwide. Epidemiological studies suggest that exposure to environmental endocrine-disrupting chemicals (EDCs) may be linked to carotid atherosclerosis, but findings are inconsistent and have not been systematically summarized. This study aimed to clarify the association between EDC exposure and carotid atherosclerosis. Methods: We searched PubMed, Web of Science, and Scopus from inception to November 23, 2024, for observational studies assessing the relationship between EDC exposure and carotid intima-media thickness (CIMT) or carotid plaque. The converted effect sizes were synthesized using random effects meta-analysis models. Methodological quality, heterogeneity, and publication bias were evaluated using the Newcastle-Ottawa scale, I2 statistics, Begg's test, and Egger's test. Results: Thirty-six studies were included in this meta-analysis. The pooled-estimate effect sizes showed that population exposure to phthalates (OR: 2.27, 95 % CI: 1.05 to 4.93), perfluoroalkyl substances (MD: 3.49, 95 % CI: 1.05 to 5.93), persistent organic pollutants (MD: 2.43, 95 % CI: 1.45 to 3.41), cadmium (MD: 7.25, 95 % CI: 1.09 to 13.42), and mercury (MD: 4.63, 95 % CI: 0.02 to 9.25) were positively correlated with CIMT. On the other hand, exposure to persistent organic pollutants (OR: 1.10, 95 % CI: 1.06 to 1.14) and arsenic (OR: 1.46, 95 % CI: 1.11 to 1.94) increased the risk of carotid plaque. Conclusion: This study revealed that EDCs were potential risk indicators for carotid atherosclerosis. Nonetheless, the sensitivity analysis results of some of the meta-analyses were not stable and demonstrated high heterogeneity. The evidence for these associations is limited, and more large-scale population-based and longitudinal studies are required to confirm these findings.
https://doi.org/10.1016/j.envres.2025.123309

Phthalates, bisphenols, and childhood allergic Phenotypes: Findings from two birth cohort studies,
Boissiere-O'neill, T., Lazarevic, N., Ponsonby, A. L., Sly, P. D., Chen, A. M., Blake, T. L., Brook, J. R., Du Berry, C., King, L., Mandhane, P. J., Moraes, T. J., Simons, E., Subbarao, P., Vilcins, D., Grp, C. I. and Grp, B. I. S. I., *Environmental Pollution*, Jan 15 2026, Vol. 389.

Phthalates and bisphenols may contribute to childhood allergic outcomes, but whether these are differentially associated with atopic or non-atopic phenotypes is uncertain. We investigated whether early-life exposure to these chemicals differentially impacts atopic and non-atopic allergic outcomes. We used two birth cohorts to investigate late pregnancy and early childhood exposure windows. The Barwon Infant Study (n = 797) in Australia measured urinary phthalate and bisphenol metabolites at 36 weeks' gestation. The Canadian Healthy Infant Longitudinal Development Study (n = 993) measured phthalate metabolites at 3, 12, and 36 months. Atopy was assessed using skin prick tests at 4-5 years. Outcomes included asthma, wheeze, eczema, and rhinitis at 4-5 years. Models were stratified by atopy. We modelled exposure mixtures using quantile G-computation and Bayesian Kernel Machine Regression. Prenatal mono-carboxy-propyl phthalate was suggestively associated with non-atopic asthma (adjusted risk ratio [aRR] = 1.12; 95 % confidence interval [CI]: 0.99-1.27) with evidence of effect modification by atopy (p for interaction = 0.02). Prenatal bisphenol A was inversely associated with overall wheeze (aRR = 0.64; 95 % CI: 0.44-0.94). In the postnatal period, diethyl and dibutyl phthalates were associated with non-atopic asthma, but not with atopic asthma, though estimates did not differ substantially by atopic status. Prenatal phthalate mixtures were more strongly associated with non-atopic asthma (aRR = 1.83; 95% CI: 1.10-3.04), with evidence of effect modification by atopy (p = 0.02 for interaction). Postnatal phthalate mixtures were associated with non-atopic asthma (aRR = 1.82, 95 % CI: 1.19-2.78), but

not atopic asthma, though the association did not differ by phenotype (p for interaction = 0.45). Phthalate mixtures showed Ushaped (prenatal) and inverse U-shaped (postnatal) associations with atopic asthma, and linear positive associations with non-atopic asthma. There was little evidence of associations for other allergic outcomes. Early-life exposure to phthalates may differentially influence the risk of childhood atopic and non-atopic asthma.
https://doi.org/10.1016/j.envpol.2025.127401

Altered sex ratio at birth after installation of a tap-water supply system in an arseniasis-endemic area in southwestern Taiwan,
Chen, C. C., Ho, S. C. and Yang, C. Y., *Journal of Toxicology and Environmental Health-Part a-Current Issues*, 2025.

Sex ratio at birth (SRB) is a simple, noninvasive way to monitor population reproductive health. Some metals might function as endocrine-disrupting chemicals (EDCs) with known estrogenic or androgenic effects and were reported to potentially influence SRBs. The metal arsenic (As) is a major risk factor for blackfoot disease (BFD), a peripheral vascular disease, endemic to southwest Taiwan for more than 50 years attributed to residents' consumption of local artesian well water, which contained high levels of this metal. In the early 1960s, a tap water supply system was implemented in BFD-endemic areas. By the mid-1970s, individuals residing in the areas had stopped using artesian well water for drinking or cooking. The aim of this study was to investigate the effects of long-term exposure to As in drinking water on the SRBs. Annual numbers of male and female births were obtained from Taiwan's Department of Household Registration, Ministry of Interior Affairs. Sex ratios at birth were calculated for BFD-endemic areas for the years from 1947 to 2024. Compared to the entire Taiwan, the BFE-endemic area displayed an odds ratio (OR) of 0.9966 (95% CI = 0.9804-1.013) for producing a male child between 1947 and 1980. However, from 1980 onwards, the OR for having a boy was significantly increased in the areas (OR = 1.0311, 95% CI = 1.0114-1.0512) compared to the time residents imbibed water from artesian well water containing high amounts of As (1947-1980). These findings provide increasing evidence that As exposure produced changes in SRBs in Taiwan. https://doi.org/10.1080/15287394.2025.2586699

Prenatal exposure to endocrine-disrupting chemicals and childhood atopic dermatitis: epidemiological evidence,
Chen, Y. X., Zhang, L., Yang, T. and Chen, L. M., *Frontiers in Microbiology*, Oct 29 2025, Vol. 16.

Atopic Dermatitis (AD) is a highly prevalent chronic inflammatory disease in children, and its global prevalence is continually rising. However, data from the past decade indicate that this overall trend masks a disparity: while the prevalence has plateaued in high-income countries, it has shown a significant upward trend in low- and middle-income countries. Prenatal exposure to endocrine-disrupting chemicals (EDCs) is an environmental factor of growing scientific concern. Key EDCs of interest include per- and polyfluoroalkyl substances (PFAS), phenolics such as bisphenol A (BPA), parabens, and triclosan (TCS), as well as phthalate esters (PAEs). Although epidemiological studies indicated an association between prenatal EDCs exposure and an increased risk of offspring developing AD, key challenges remain unresolved, including population heterogeneity, methodological variations in exposure assessment, and elucidation of the underlying mechanisms. The review summarized the epidemiological evidence linking prenatal EDCs exposure to childhood AD, aiming to provide a theoretical basis for the early prevention of AD. Furthermore, it highlighted the future need to integrate multi-omics technologies with prospective cohort studies to elucidate the effects of mixed EDCs exposures and identify critical intervention windows.
https://doi.org/10.3389/fmicb.2025.1681214

Systematic literature review and meta-analysis on the reproductive effects of micro- pollutants in humans and animals,
Coppeta, L., Ferrari, C., Ippoliti, L., Campagnolo, L. and Magrini, A., *Frontiers in Toxicology*, Nov 19 2025, Vol. 7.

Background: Micro-pollutants, such as particulate matter, heavy metals, endocrine-disrupting compounds, and persistent organic pollutants, raise significant concerns regarding reproductive health in both humans and animals. Methods: This systematic review and meta-analysis, conducted according to PRISMA guidelines, assessed available evidence on micro-pollutant exposure and reproductive outcomes. Out of 2,134 records identified, 52 studies (31 human, 21 animal) met inclusion criteria. Results: Exposure to micro-pollutants was consistently associated with adverse reproductive outcomes. Human studies reported increased risks of irregular menstruation, preterm delivery (OR = 1.42), intrauterine growth restriction (OR = 1.36), and reductions in sperm concentration (SMD = -0.48) and testosterone levels. A meta-analysis of 23 studies confirmed these associations, while animal studies provided mechanistic support, including histological damage and epigenetic modifications. Despite substantial heterogeneity, the overall quality of included studies was moderate-to-high. Conclusion: Evidence indicates that micro-pollutants are strongly associated with impaired reproductive health. While causality cannot be definitively established due to observational study designs, the consistency of findings across populations, pollutants, and species highlights an urgent need for further research and regulatory measures to mitigate reproductive risks. https://doi.org/10.3389/ftox.2025.1671098

Systematic Review and Meta-Analysis on Heavy Metals and Trace Elements in Mild Cognitive Impairment,
Dong, Y., Ren, L., Tang, T., Zhang, X., Han, D., Luo, Y., Wang, L., Cui, Z., Ji, S., Zheng, J. and Qing, Y., *Biol Trace Elem Res*, Dec 26 2025.

Mild cognitive impairment (MCI) represents a prodromal stage of various neurodegenerative diseases. However, heterogeneity persists regarding heavy metal and trace element levels in MCI patients. PubMed, Web of Science, and Chinese academic databases were systematically searched from 2000 to the present, and 43 case-control/cross-sectional studies on the levels of heavy metals and trace elements in MCI and healthy controls were included, and the standardized mean difference (SMD) of 12 elements (Al, As, Cd, Pb, Cu, Se, Zn, etc.) was evaluated by using a random-effects model. A total of 16,743 samples were included. Al (SMD: 0.73, 95%CI: 0.31-1.14), As (SMD: 0.19, 95%CI: 0.03-0.35), Cd (SMD: 0.91, 95%CI: 0.43-1.38), Cu (SMD: 0.69, 95%CI. 0.27-1.10), Pb (SMD: 0.77, 95%CI: 0.30-1.24) were significantly elevated in the MCI patients, while Se (SMD: -0.28, 95%CI: -0.56-0.01) and Zn (SMD: -0.77, 95%CI: -1.22-0.33) were significantly lower. No statistical differences were observed for the remaining elements (Fe, Mg, etc.). Levels of specific heavy metals and trace elements in MCI patients differ from those in healthy controls. Monitoring and modulating these element levels may provide novel targets for early intervention strategies.
https://doi.org/10.1007/s12011-025-04941-2

Association of Exposure to Phthalate Metabolites with Antenatal Depression in US Pregnant Women,
Dubey, P., Thangavel, C., Yousif, A., Kim, S. and Reddy, S., *Toxics*, Sep 30 2025, Vol. 13, no. 10.

Antenatal depression affects 10-20% of pregnant women, with notable adverse outcomes for the neonates. Limited studies have indicated a potential link between exposure to phthalate metabolites and depression. The association between phthalate metabolites and depression in pregnant women is unknown. We sought to evaluate the association of exposure to phthalate

metabolites with depression severity score in US pregnant women. This cross-sectional study used data collected by the National Health and Nutrition Examination Survey during 2005-2018 on pregnant adults who completed urinary profiles that examined 12 common phthalate metabolites. Linear and quantile sum regressions were used to evaluate the association between depressive symptoms (measured by the Patient Health Questionnaire, PHQ-9) and concentrations of phthalate metabolites. A total of 208 women were included in the analysis. These women's mean (SD) age was 27.42 (5.78) years. We found that all the phthalates were associated with PHQ-9 scores except for mono (carboxyoctyl) and mono-isononyl phthalate. Similar results were observed with the association of high levels of phthalates with mild, moderate, and severe depression (PHQ-9 >4 vs. <= 4). All the phthalate metabolites remained significantly associated with depression scores in the adjusted analysis. Among all considered phthalate metabolites, a combination of MCNP, MBP, MiBP, MnBP, and MEHP contributed to the strongest association with higher depression scores. The relative importance was similar for MCNP (weight = 0.32) and MBP (weight = 0.31), followed by MiBP (weight = 0.12), MnBP (weight = 0.08), MEHP (0.07), and MEP (weight = 0.04) for depression scores. Our findings suggest that pregnant women with high exposure to phthalates are more likely to have higher depressive symptom scores. https://doi.org/10.3390/toxics13100838

The influence of environmental and chemical exposures on fertility in the Eastern Mediterranean region: A narrative review,
Fares, K. S., Tayeh, G. H. A., Whaibeh, E. R., Jaalouk, L. Y., Matar, Y. M. and Mrad, M. A., *International Journal of Reproductive Biomedicine*, Oct 2025, Vol. 23, no. 10, p. 787-802.

Infertility has increasingly become a global medical challenge. Environmental exposures have been suggested to interfere with reproduction. This review focuses on the impacts of climate and chemical exposures on reproductive functions and assisted pregnancy outcomes in the Eastern Mediterranean region. The search strategy was applied to PubMed and Scopus databases including publications from January 2012-June 2024. 63 studies investigating climatic factors, chemical exposures, trace elements, and smoking among the Eastern Mediterranean region population were included. Around 59% (n = 37) and 36% (n = 23) of the analyzed publications evaluated male factors and female factors, respectively. A decrease in sperm parameters was correlated to high temperatures, bisphenol A, and air dust exposures. Men endocrine reproductive system is negatively affected by phthalates and pesticides containing products. Trace elements showed a double role regarding reproduction. Heavy smokers were found to have poorer semen quality compared to regular smokers. The available evidence summarizing environmental exposures and smoking habits, and infertility assistance outcomes is limited and inconsistently distributed across the studied region. Addressing the vast health disparities and cultural and social discrepancies within the region can enhance public awareness, education, policy, and regulation development. https://doi.org/10.18502/ijrm.v23i10.20313

Exploring the association between brominated flame retardant exposure and the risk of rheumatoid arthritis: A comprehensive analysis,
Feng, X. B., Tang, B. R., Xia, H., Zhang, Y., Zheng, L., Wang, Y. J., Wang, M., Liang, R. Y. and Yan, C. X., *Ecotoxicology and Environmental Safety*, Nov 1 2025, Vol. 306.

Brominated flame retardants (BFRs), widely used for their flame-retardant properties, have raised global health concerns. Given the limited evidence linking BFRs to rheumatoid arthritis (RA), we investigated the association between BFR exposure and RA, as well as the role of immune-inflammatory responses. This study recruited 9908 general adults. Serum BFRs, including 8 polybrominated diphenyl ethers (PBDEs) and 2,2',4,4',5,5'-Hexabromobiphenyl (PBB153), were measured to evaluate exposure levels. The pan-immune-inflammation value (PIV) and neutrophil-to-

lymphocyte ratio (NLR) were calculated to assess immune-inflammatory response. The logistic regression model and generalized linear model were used to estimate the associations of individual and mixed BFRs with RA and immune-inflammatory indicators. Mediation analyses and toxicogenomic bioinformatics analyses were conducted to explore the underlying mechanism. Specific PBDE congeners (PBDE85, 100, 153, 154, 209) and PBB153 showed significant dose-dependent associations with an increased risk of RA (all P trend<0.05). Doubling the concentration increases in these compounds elevated RA risk by 10 %-21 %. Mixed BFR exposure also significantly increased the risk of RA, with PBB153 showing the highest contribution weight. PBDE85 and PBDE154 were positively associated with increased PIV or NLR in a dose-response manner (P and P trend<0.05). PIV or NLR partially mediated the associations of PBDE85 and PBDE154 with RA risk. The toxicogenomic bioinformatics analyses further indicated the important role of regulation of immune-inflammatory response in linking BFR exposure to RA. Overall, BFR exposure was associated with an increased risk of RA, and immune-inflammatory responses may contribute to the pathogenesis of BFR-associated RA. https://doi.org/10.1016/j.ecoenv.2025.119338

Perchlorate and thyroid function,
Handler, S. N., Cuadros, M. a. L. and Pearce, E. N., *Current Opinion in Endocrine and Metabolic Research*, Dec 2025, Vol. 41.

Perchlorate is an environmental contaminant found around the world. Perchlorate disrupts thyroid function by inhibiting the sodium iodide symporter, which transports iodide into the thyroid. The impact of perchlorate on thyroid function is of particular concern during gestation. This review focuses on human studies related to the thyroidal effects of perchlorate. Some of the earliest human studies of perchlorate and thyroid function studied high-dose exposure through randomized control trials and occupational studies. These gave way to epidemiologic and cohort studies focusing on environmental exposures. The results of these studies have been variable but suggest that high levels of environmental perchlorate exposure, particularly in the setting of iodine deficiency, may impair thyroid function and fetal neurological development. Regulatory efforts have been supported by the advent of biologically dose-dependent response models. Understanding this body of the literature is critical for developing policies aimed at regulating perchlorate exposures and protecting society's most vulnerable populations. https://doi.org/10.1016/j.coemr.2025.100589

Sex-Specific Associations of Early Life Exposure to the Pesticide Mixture with Cardiometabolic Outcomes in CHAMACOS Young Adults,
Hu, C. Y., Mora, A. M., Gunier, R. B., Rauch, S., Kogut, K., Gregory, J. K., Erkin-Cakmak, A., Eskenazi, B. and Rosa, M. J., *Environmental Science & Technology*, Nov 11 2025, Vol. 59, no. 44, p. 23702-23713.

Agricultural pesticide exposure has been linked to cardiometabolic health, but little is known about the long-term effects of exposure to pesticide mixtures during sensitive developmental periods. We examined prenatal and early childhood exposure to agricultural pesticide use within one km of residences in the CHAMACOS cohort (n = 505) in California's Salinas Valley. Twelve pesticides commonly applied in the region between 1999 and 2007 were included. At the age of 18 years, participants underwent clinical assessments of body mass index, waist circumference, insulin resistance, blood lipids, liver enzymes, and the presence of metabolic syndrome. Mixture associations were evaluated using statistical methods for correlated exposures, and single-pesticide models were examined separately. Analyses accounted for potential confounders and were stratified by sex. Higher early childhood exposure to the pesticide mixture was associated with increased odds of metabolic syndrome in males (OR = 1.76; 95% CI: 1.06, 2.05) but not females (OR = 0.87; 95% CI: 0.53, 1.26). Findings suggest that early life exposure to agricultural pesticide

mixtures may contribute to adverse cardiometabolic outcomes in young men, underscoring the importance of considering sex-specific susceptibility in environmental health research.
https://doi.org/10.1021/acs.est.5c06486

Bisphenol A and human fertility: a systematic review,
Isa, C. P. M., Schmidt, G. B., De Jesus, R. G., Sturmer, J., De Castilhos, J. P., Chapochnicoff, L. R., Dornelles, V. C., Hentschke, M. R., Petracco, A. and Badalotti, M., *Jornal Brasileiro De Reproducao Assistida*, Oct-Dec 2025, Vol. 29, no. 4, p. 806-811.

Considering the significant exposure to the synthetic compound bisphenol A (BPA), present in a wide range of materials in our daily lives, this article discusses a possible correlation between this substance and human fertility through a bibliographic review. In the context of growing evidence that BPA impacts the fertility of women and men of reproductive age, the reviewed articles suggest that exposure to this agent may affect ovarian reserve parameters in women. In pregnant women, it may cause fetal malformations. BPA has also been linked to an increase in spontaneous abortions and premature births. Additionally, it can cause hormonal disruptions, affect folliculogenesis, and worsen ovarian response in assisted reproduction, as well as lead to lower estradiol concentrations, reduced fertilization rates, and higher implantation failure. In men of reproductive age, BPA may decrease sperm production, potentially contributing to testicular dysgenesis syndrome and cryptorchidism. However, further studies are still required to better understand the diverse and complex mechanisms through which BPA affects key reproductive functions.
https://doi.org/10.5935/1518-0557.20250029

Associations of urinary environmental phenols with obesity and lipid metabolism in children and adolescents: The expanded Chinese National Human Biomonitoring (CNHBM) project,
Jiang, N., Chen, Q., Cheng, B. J., Meng, K., Wang, J., Li, T. L., Chen, H., Liao, Y. H., Sun, H. and Liu, R., *Environmental Research*, Jan 1 2026, Vol. 288.

Despite ubiquitous exposure to environmental phenols (EPs), their associations with obesity are poorly understood due to inconsistent findings and inadequate mechanistic insights. Within the China National Human Biomonitoring program, we measured 15 urinary EPs in 860 children/adolescents from Jiangsu Province, employing lipidomics to investigate obesity associations. EPs were detectable in 17.93 %-96.79 % samples, with Bisphenol B (BPB) and benzophenone-4 (BP-4) emerging as predominant compounds. Urinary EPs concentrations correlated significantly with sex, BMI status, household income, and dietary patterns. Multivariable logistic regression showed a linear inverse association between BPB and BP-4 exposure and overweight/obesity in pubertal girls. Bayesian Kernel Machine Regression (BKMR) and Quantile g-computation (QGC) analyses confirmed that urinary EPs were inversely associated with overweight/obesity in the overall cohort (OR = 0.76, 95 % CI: 0.59-0.98) and among girls (OR = 0.63, 95 % CI: 0.44-0.90). Lipidome-wide association studies (LWAS) applied generalized linear models (GLMs) with Gaussian and binomial distributions to evaluate the relationships of EP concentrations and overweight/obesity status with lipid abundances, identifying 28 metabolites and 10 pathways that link EPs exposure to overweight/obesity. Mediation analyses indicated BP-4 effects were partially mediated by glycerophospholipid (-6 % to -13 %) and sphingolipid metabolites (9 %-18 %), whereas BPB effects were driven by sphingolipid (7 %-8 %). Stratified analyses indicate that alterations in glycerophospholipid and sphingolipid pathways mediate sex-specific EPs effects on overweight and obesity, providing a theoretical basis for targeted public health strategies.
https://doi.org/10.1016/j.envres.2025.123297

Neuroprogramming of prenatal phthalate exposures on fluid cognition: A latent variable modeling approach to quantify exposure burden and integrate neurobehavioral data,
Lane, J. M., Cohen, N., Midya, V., Alcala, C. S., Eggers, S., Martinez-Medina, S., Valvi, D., Téllez-Rojo, M. M., Cory-Slechta, D. A., Wright, R. O. and Liu, S. H., *Neurotoxicology and Teratology*, Jan-Feb 2026, Vol. 113.

Background: Phthalates are endocrine-disrupting chemicals with neuroactive properties linked to maladaptive neurodevelopment in children. However, few studies have utilized latent variable methodologies to estimate their cumulative impact and assess the complex integration of cognitive processes that characterize fluid cognition-the ability to efficiently process, manipulate, and integrate information to solve reasoning problems. Objective: We investigated the prenatal trimester-specific neuroprogramming effects of the phthalate burden scores on fluid cognition in Mexican children. Methods: Children (n = 626) aged 6-7 years from a prospective pregnancy cohort in Mexico City were administered subtests from the CANTAB, completing the between error, strategy, and mean latency measures intended to evaluate a broad spectrum of cognitive domains representative of fluid cognition. Phthalate metabolites were measured in maternal urine collected at 2nd and 3rd pregnancy trimesters. A CFA validated and quantified two correlated latent phthalate burden scores representing prenatal exposure to low molecular weight (LMW) and high molecular weight (HMW) phthalates. Trimester-specific models using a covariate-adjusted SEM estimated the associations of latent phthalate burden scores with a latent construct of fluid cognition, an integration of working memory, executive function, and attention tasks. Results: In the 3rd trimester, higher LMW phthalate burden was associated with poorer fluid cognition (b = -1.860; [95 % CI = -3.505, -0.215]; p = 0.027), while HMW phthalate burden showed a positive association (b = 1.815; [95 % CI = 0.176, 3.453]; p = 0.030). Conversely, in the 2nd trimester, neither burden levels of LMW (b = -0.508; [95 % CI = -1.639, 0.623]; p = 0.378) nor HMW (b = 0.451; [95 % CI = -0.671, 1.573]; p = 0.431]; p = 0.44) phthalate demonstrated significant associations with fluid cognitive performance. Conclusion: The temporal sensitivity of prenatal phthalate exposures on fluid cognition showed effects in later stages, with higher LMW burden linked to poorer performance and HMW burden showing a positive association. Our findings emphasize latent variable approaches and the need for more research on exposure-driven integrated cognitive programming.
https://doi.org/10.1016/j.ntt.2025.107575

Heavy metal exposure and its impact on inflammatory ratios in minors: The mediating role of BMI,
Li, X. and Han, L., *PLoS One*, 2025, Vol. 20, no. 12, p. e0339470.

BACKGROUND: Despite existing evidence that endocrine-disrupting chemicals like heavy metals exposure impairs health of minors, the association between the exposures and inflammatory ratios remains uncertain. This study aims to investigate the relationship between heavy metal exposure and inflammatory ratios, focusing on BMI as a potential mediator in this association. METHOD: We conducted a retrospective cross-sectional analysis from the NHANES 2007-2018. 14,007 minors were categorized into different age groups, and analyses were performed based on demographic characteristics. Multiple linear regression and mediation analysis were applied to asses associations between heavy metal concentrations and inflammatory ratios, with BMI included as a mediating variable. RESULTS: The participants were divided into four age groups: toddlers (2487), preschool children (2297), school-age children (5019), and teenagers (4204). Blood Pb was positively correlated with LMR (β = 0.70, 95% CI: 0.60-0.81) and PNR (β = 14.88, 95% CI: 12.29-17.47), with 25.89% and 27.02% of these associations mediated by BMI. Negative correlations were observed between Pb and inflammation ratios, including NLR (β = -0.29, 95% CI: -0.34 - -0.24), PLR (β = -10.35, 95% CI: -12.61- -8.08), and NMR (β = -0.63, 95% CI: -0.78 - -0.48), with BMI accounting for 37.64%,

22.40%, and 39.59% of these effects, respectively. Blood Cd and Hg were also correlated with these ratios, with BMI consistently mediating these associations. CONCLUSIONS: BMI serves as a significant mediator between blood heavy metals and inflammatory ratios among minors.
https://doi.org/10.1371/journal.pone.0339470

Risk factors for hypospadias: a prospective single-center study from Ghana,
Maison, P. O. M., Appiah, K. a. A., Arthur, D., Amoabeng, J., Mensah, P. and Arthur, A., *World Journal of Urology*, Nov 22 2025, Vol. 43, no. 1.

Introduction Hypospadias is a common congenital defect in boys, though its causes are mostly unknown, likely arising from genetic and environmental factors. We analyzed hypospadias cases at our center to identify prevalence of risk factors. Methods We collected data prospectively on boys with hypospadias and their parents who visited our center from January 2023 to December 2024. The urology unit diagnoses two new cases of hypospadias each month. Therefore, 51 patients were recruited, expecting 5% of the data to be unusable. Data collected and analyzed included the child's gestational age, birth weight, type of hypospadias, associated abnormalities, parents' ages, exposure to organophosphate pesticides and phytoes-trogens, maternal contraceptive use during pregnancy, and a history of subfertility or hypospadias in the father. Results This study involving 51 boys aged 2 months to 11 years with hypospadias and their parents revealed that 84.3% were born at term, while 45.1% had low birth weights, with no correlation between birth weight and hypospadias type (p = 0.35). Most mothers (54.9%) and fathers (86.3%) were 30 or older at birth, and 45.1% of mothers and 27.5% of fathers frequently consumed phytoestrogen-rich foods. Exposure to organophosphate pesticides was noted by 17.6% of mothers and 11.7% of fathers. During pregnancy, 15.7% of mothers used oral contraceptives and 5.9% used progestogens. Among fathers, 11.7% had a history of subfertility, and 3.9% had cryptorchidism, with no father having hypospadias. Conclusion Low birth weight, advanced parental age, and exposure to phytoestrogens and organo-pesticides are associated with hypospadias in our patients
https://doi.org/10.1007/s00345-025-06091-5

Prenatal and prepubertal exposures to organochlorine compounds and perfluoroalkyl substances and pubertal development at age 12: The PELAGIE cohort study,
Menant, L., Rouget, F., Tillaut, H., Warembourg, C., Rouxel, E., Lainé, F., Gaudreau, É., Cordier, S., Garlantézec, R., Monfort, C. and Chevrier, C., *Environment International*, Nov 2025, Vol. 205.

Background: Emerging evidence suggests that prenatal and prepubertal exposure to organochlorine compounds (OCs) and perfluoroalkyl substances (PFASs) is associated with children's reproductive health. This study examines the potential impact of these exposures on pubertal development in 12-year-old children. Methods: Based on the French PELAGIE mother-child cohort, concentrations of OCs and PFASs were measured in cord blood (from 2003 to 2006) and in blood at age 12 (from 2016 to 2018). Medical staff assessed pubertal development (Tanner stages) at age 12, and girls self-reported age at menarche annually (ages 9-16). Associations between exposures and delayed or earlier pubertal development were analyzed using multinomial logistic and Cox regression models, adjusting for confounders, and using quantile g-computation for compound mixtures. Results: Among 502 children (250 girls, 252 boys; median age: 12.8 years), prenatal PFUdA exposure in girls was associated with delayed breast development [OR (95 %CI): 2.05 (1.03,4.06)]. In boys, prenatal PFHxS exposure was associated with reduced risk of earlier gonadal development [0.47 (0.26,0.83)], and beta-HCH with reduced risks of both delayed [0.66 (0.43,0.99)] and earlier [0.69 (0.48,0.97)] pubic hair development. Prepubertal exposure in girls to HCB, PCBs, and PFASs was associated with increased risk of delayed breast development [e.g., PFOA: 2.53 (1.04,6.12)] and later age at menarche [e.g., Sigma PCBs: HR 0.77 (0.61,0.97)]. In boys, prepubertal p,p'-DDE was associated with

increased risk of earlier puberty [gonadal development: 1.77 (1.09,2.88); pubic hair growth: 1.56 (1.01,2.44)], while PCB-118 was associated with delayed development. Prepubertal PFASs were associated with reduced risk of earlier puberty [e.g., PFHxS-gonadal stages: 0.39 (0.20,0.75)]. In mixture analyses, no associations were observed with regards to prenatal exposure, but prepubertal exposure was associated with delayed pubertal development in girls. Conclusion: Prenatal and prepubertal exposure to OCs and PFASs may alter pubertal development at age 12 in girls and boys, underscoring the need for further research. https://doi.org/10.1016/j.envint.2025.109845

Évaluation de l'exposition ubiquitaire aux perturbateurs endocriniens,
Mirakian, P. and Pretalli, J.-B., *Actualités Pharmaceutiques*, 2026/01/01/ 2026, Vol. 65, no. 652, p. 16-20.

Le questionnaire Fertilyon est simple et rapide. Il permet d'évaluer l'exposition quotidienne aux perturbateurs endocriniens, notamment chez les personnes prises en charge pour infertilité. Les différentes sources possibles d'exposition sont considérées (alimentation, cosmétiques, plastiques, etc.). Il s'agit d'un outil épidémiologique mais aussi pédagogique particulièrement utile pour sensibiliser les patients. Assessment of ubiquitous exposure to endocrine disruptors The Fertilyon questionnaire is quick and easy to complete. It assesses daily exposure to endocrine disruptors, particularly in people undergoing infertility treatment. The various possible sources of exposure are considered (food, cosmetics, plastics, etc.). It is both an epidemiological and educational tool, particularly useful for raising patient awareness.
https://doi.org/10.1016/j.actpha.2025.10.009

Lien entre perturbateurs endocriniens et infertilité,
Mirakian, P. and Pretalli, J.-B., *Actualités Pharmaceutiques*, 2026/01/01/ 2026, Vol. 65, no. 652, p. 21-24.

Les perturbateurs endocriniens nuisent à la santé, notamment reproductive. Leurs effets sont parfois irréversibles, surtout si l'exposition est prénatale. Les dosages de ces polluants ubiquitaires sont coûteux et complexes en routine, et ils n'identifient ni leur effet cocktail ni la durée d'exposition. Dans le cadre d'une étude, un questionnaire a été utilisé pour évaluer les expositions des couples infertiles et les informer sur les comportements les plus sains. Link between endocrine disruptors and infertility Endocrine disruptors are harmful to health, particularly reproductive health. Their effects are sometimes irreversible, especially if exposure occurs during the prenatal period. Routine testing for these ubiquitous pollutants is costly and complex, and does not identify their cocktail effect or the duration of exposure. As part of a study, a questionnaire was used to assess the exposure of infertile couples and inform them about the healthiest behaviors.
https://doi.org/10.1016/j.actpha.2025.10.010

Neurodevelopment in children born to women exposed to pesticides during pregnancy,
Mwakalasya, W. N., Mamuya, S. H., Manji, K., Moen, B. E. and Ngowi, A. V., *PLoS One*, 2025, Vol. 20, no. 12, p. e0326007.

The global rise in pesticide use, particularly across Africa, raises concerns about maternal occupational exposure during pregnancy and its potential impact on child neurodevelopment. This study examined associations between self-reported maternal pesticide exposure during pregnancy and neurodevelopmental outcomes in children aged 4-6 years. A cross-sectional design was implemented, comprising 432 mother-child pairs from three horticulture-intensive regions in Tanzania. Maternal exposure was assessed through structured interviews, focusing on activities during pregnancy such as pesticide spraying, weeding, and handling contaminated clothing.

Children's neurodevelopment was evaluated using the International Development and Early Learning Assessment (IDELA), which measures motor skills, literacy, numeracy, social-emotional development, and executive function. Linear regression analyses revealed that children of mothers who reported pesticide spraying during pregnancy scored significantly lower in social-emotional (β = -6.813, 95% CI: -11.53 to -2.096, p = 0.005) and executive function (β = -9.317, 95% CI: -16.007 to -2.627, p = 0.006) domains. Overall, children achieved the highest mean scores in fine and gross motor skills (62.11 ± 19.3) and the lowest in executive function (43.97 ± 24.3). Age-related differences were also observed, with six-year-olds consistently outperforming younger children across all developmental domains. These findings suggest an association between maternal pesticide exposure during pregnancy and adverse neurodevelopmental outcomes in offspring. Given that exposure data were self-reported, results should be interpreted cautiously. Nevertheless, the study underscores the urgent need for comprehensive risk assessments incorporating objective exposure measurements, particularly in horticultural settings where women of reproductive age represent a substantial proportion of the workforce. https://doi.org/10.1371/journal.pone.0326007

Urinary concentrations of di-butyl phthalate isomers and reproductive hormonal parameters in adult men: A systematic review with dose-response meta-analysis,
Nita, T. M., Vernez, D., Wild, P., Pitteloud, N. and Hopf, N. B., *Environmental Toxicology and Pharmacology*, Jan 2026, Vol. 121.

Background: Male reproductive decline has been linked to phthalate exposure. Di-butyl phthalate isomers (DnBP and DiBP) are endocrine disruptors with inconsistent evidence regarding effects on the hypothalamic-pituitarygonadal/thyroid (HPG/T) axis. Objective: To perform a dose-response meta-analysis of associations between DnBP and DiBP exposure and HPG/ T-axis hormones. Methods: Five databases were searched. The associations between urinary DBP metabolite concentrations (monon-butyl phthalate [MnBP], mono-iso-butyl phthalate [MiBP], or nonspecific DBP metabolites [& sum;DBPm]) and hormone levels (TT, fT, SHBG, LH, FSH, E2, INHB, and TSH) were analyzed using meta-regressions (unadjusted [UA], covariate-adjusted [CA], fertility-adjusted [FA]). Results: From 10,410 records, 19 studies (N = 12,128) were considered. MiBP was negatively correlated with LH (UA: R=-0.117, p = 0.02; CA: R=-0.094, p = 0.012; FA: R=-0.125, p = 0.009), positively with E2 (CA: R=0.084, p = 0.045), and SHBG (CA: R=0.09, p = 0.034; FA: R=0.091, p = 0.015). MnBP was positively associated with TSH (UA: R=0.152, p = 0.001; CA: R=0.188, p = 0.006). Conclusions: DBP-isomers exposure is associated with altered HPG/T-axis hormone levels. https://doi.org/10.1016/j.etap.2025.104900

Mass spectrometry-based untargeted metabolomics study of polycystic ovary syndrome,
Özer, Ö., Ibrahimoglu, A. Z., Gül, A. Z., Demirel, M., Ates, S., Taha, H. S., Ibrahimoglu, M. and Selek, S., *Journal of Ovarian Research*, Nov 12 2025, Vol. 18, no. 1.

BackgroundPolycystic ovary syndrome (PCOS) is a complex endocrine and metabolic disorder, and its diagnosis remains controversial due to heterogeneous phenotypes and varying diagnostic criteria. Insulin resistance and its metabolic consequences are central features of PCOS management. Metabolomics has increasingly been applied to elucidate the pathophysiology of complex disorders. In this study, we sought to determine which serum metabolites and metabolic pathways are differentially altered in women with PCOS compared with healthy controls, thereby addressing whether metabolomic profiling can reveal candidate biomarkers for early diagnosis and potential therapeutic targets.MethodsFifty patients diagnosed with PCOS and 50 healthy controls matched for age and body mass index (BMI) were included in the study. Blood samples were collected for metabolomic analysis and routine biochemical parameters. Metabolomic analysis was performed by UPLC-HRMS and data were processed using MZmine, TidyMass and MetaboAnalyst.

Metabolite annotation was performed using databases such as HMDB, MassBank and MoNA.ResultsMetabolomic analysis revealed 49 compounds in the serum of PCOS patients, 39 of which were upregulated and 10 of which were downregulated. Compounds such as di(2-ethylhexyl) phthalate (DEHP), promethazine N-oxide, tetrahydromagnolol, 5-methyl-5-phenylhydantoin, valerenic acid, butylparaben, erucamide, DDAO, d-erythro-sphinganin-1-phosphate and 1-arachidoyl-2-hydroxy-sn-glycero-3-phosphocholine were significantly higher in the PCOS group. Compounds such as L-methyladenosine, cystine, glu-gln and 2,2'-methylene-bis(6-tert-butyl-4-methylphenol) were significantly lower. In the pathway analysis performed using KEGG database, sphygolipid metabolism, sphygolipid signaling pathway, neuroactive ligand-receptor interaction and phenylalanine metabolism were found to be the most affected pathways.ConclusionThis study demonstrates distinct alterations in lipid and amino acid metabolism in PCOS and highlights the accumulation of exogenous molecules, including endocrine disruptors, in patient serum. By integrating metabolomic profiling with clinical phenotyping, our findings provide novel insights into PCOS pathophysiology and suggest potential serum biomarkers that may support early diagnosis and personalized therapeutic approaches. https://doi.org/10.1186/s13048-025-01842-9

Linking Pesticide Exposure to Gestational Diabetes: Current Knowledge and Future Directions, Pagkaki, C., Tsikouras, P. and Halvatsiotis, P., *Physiologia*, 2026, Vol. 6, no. 1, p. 4. https://www.mdpi.com/2673-9488/6/1/4

Preconception, gestation, and childhood exposure to air pollution and risk of polycystic ovary syndrome (PCOS) in a US girls cohort study,
Peebles, E., Mitsunami, M., Zhang, B. Y., Chen, J., Coull, B. A., James-Todd, T., Chavarro, J. E., Hart, J. E., Laden, F. and Mahalingaiah, S., *Environment International*, Nov 2025, Vol. 205.

Background: Exposure to ambient air pollution (AP) during sensitive developmental periods could dysregulate the reproductive system, resulting in later in life menstrual disorders, including polycystic ovary syndrome (PCOS). Minimal research exists examining the relationship between AP exposure and PCOS. Objectives: To determine if residential ambient particulate matter (PM) and nitrogen dioxide (NO2) exposure during preconception, gestation, and childhood increases the risk of PCOS. Methods: We used data from 3,321 female participants with gestational data available born between 1989 and 1994 in the Growing Up Today Study 2 (GUTS2), an ongoing United States (US) cohort initiated in 2004. Exposure to ambient PM (<= 2.5, 2.5-10, and <= 10 mu m) and NO2 were estimated using nationwide spatiotemporal models based on biennially updated maternal residential addresses. Conception month was estimated based on reported gestational age and participant date of birth. Preconception was defined as the three months before the estimated conception month. Gestation was defined as conception month to date of birth. The gestational period was further stratified by first, second, and third trimester, calculated from conception month and date of birth. Childhood exposure was defined as the averaged monthly exposure from birth to age at menarche. Participants self-reported PCOS via questionnaires. Hazard ratios (HR) were estimated for PCOS per interquartile range increase using Cox proportional hazard models with combined inverse probability weights. Results: In total, 7.1 % of participants self-reported a PCOS diagnosis. Exposure to PM2.5 in the first trimester showed an higher risk of PCOS (aHR 1.38 [95% CI 1.03, 1.85] per 5.4 mu g/m3). Exposure to PM2.5-10, PM10, and NO2 during preconception, gestation, and childhood showed little association of PCOS risk, with the exception of PM10 exposure during the first trimester which showed a suggestive association of higher PCOS risk (aHR 1.29 [95 % CI 0.97, 1.72] per 9.6 mu g/m3). Discussion: Higher exposure to PM2.5 in the first trimester was associated with an increased risk of PCOS.
https://doi.org/10.1016/j.envint.2025.109885

Correlation of per- and poly-fluoroalkyl substances (PFAS) exposure with testosterone levels in the male population,
Rahman, H. H., Stokey, W. R. and Munson-Mcgee, S. H., *Environ Toxicol Pharmacol*, Jan 2026, Vol. 121, p. 104906.

Human exposure to per- and poly-fluoroalkyl substances (PFAS) occurs from environmentally contaminated food and water. PFAS are a health concern because they are associated with various neurological, developmental, and endocrine disorders. Despite causes of infertility being equal, male causes are less studied, with etiologies ranging from genetic to anatomic to physiologic dysfunctions. This study aimed to investigate a correlation between six subtypes of PFAS with low male testosterone levels. Data from the National Health and Nutrition Examination Survey (NHANES) cycles 2013-2016 were utilized to assess serum PFAS and testosterone levels. This study observed age, marital status, body mass index, smoking status, alcohol consumption, and diabetic status being significantly correlated with low testosterone levels. PFNA exposure was observed to have a strong inverse relationship with male testosterone levels in low/medium (ORs 0.518, 0.571, 0.322, 0.455) and low/high-medium exposure levels (ORs 0.262, 0.262, 0.321, and 0.310), indicating exposure-dependent effects on testosterone levels. https://doi.org/10.1016/j.etap.2025.104906

Prenatal phenol exposure and child behaviour: insights into the hypothalamic–pituitary–adrenal axis from two prospective mother–child cohorts,
Rolland, M., Bustamante, M., Jedynak, P., Thomsen, C., Sakhi, A. K., Foraster, M., Gascon, M., Gómez-Roig, M. D., Llurba, E., Rivas, I., Ouellet-Morin, I., Ferrer, M., Morillas, A., Carras, S., Bayat, S., Lyon-Caen, S., Pozo, O. J., Vrijheid, M., Sunyer, J., Slama, R., Dadvand, P. and Philippat, C., *The Lancet Planetary Health*, 2025/12/01/ 2025, Vol. 9, no. 12, p. 101330.

Summary Background Synthetic phenols are widely used chemicals with potential neurodevelopmental toxicity. Human studies are often limited by small sample sizes and exposure misclassification. Identifying the biological pathways affected by these substances is crucial for understanding key drivers of toxicity. We aimed to study associations between prenatal exposure to synthetic phenols and child behaviour, exploring the potential mediating role of maternal steroid hormones. Methods We pooled data from two European cohorts: the Barcelona Life Study Cohort (BiSC; Barcelona, Spain, 2018–21, N=1080) and Suivi de l'Exposition à la Pollution Atmosphérique durant la Grossesse et Effets sur la Santé (SEPAGES; Grenoble, France, 2014–17, N=484). Mothers older than 18 years having a singleton pregnancy of less than 19 weeks gestational age were eligible for inclusion in the cohorts; those having multiple pregnancies were excluded. Repeated urine samples (up to 24 in BiSC; up to 42 in SEPAGES) collected in the second and third trimesters were pooled and analysed for 12 synthetic phenols. Child behavioural outcomes were assessed at 18 months in BiSC and 24 months in SEPAGES using the Child Behavior Checklist for Ages 1·5–5 (CBCL). Concentrations of total cortisol, total cortisone, and 11-dehydrocorticosterone—steroid hormones involved in the hypothalamic–pituitary–adrenal axis—were measured from maternal hair samples. Associations between phenol exposure and behavioural outcomes were estimated by adjusted linear regression analysis, and mediation by steroid hormones was assessed with regression-based causal mediation analysis within the counterfactual framework. Findings 1024 mother–child pairs were included in the study: 607 from BiSC and 417 from SEPAGES. Maternal exposure to methylparaben in the third trimester of pregnancy was associated with higher internalising scores (change in score of 0·44 [95% CI 0·10–0·79] points) and externalising scores (0·67 [0·12–1·24]) in the CBCL. In boys, maternal exposure to bisphenol S in the third trimester was linked to increased internalising scores (0·92 [0·15 to 1·75]; p=0·019) and could be linked to increased externalising scores (1·14 [−0·09 to 2·44]; p=0·070). In girls, second-trimester butylparaben and propylparaben exposure were associated with lower internalising (−1·03 [−1·84 to −0·09], p=0·033) and externalising (−0·68 [−1·23

to −0·12]; p=0·019) scores. No mediation by steroid hormones was observed. Interpretation Prenatal exposure to phenols might influence early behavioural development, with sex-specific patterns. There was no strong evidence of mediation by maternal steroid hormones, suggesting the involvement of alternative pathways in the biological effects of phenols. Together with previous findings, these results highlight the need for stricter regulation of these compounds to reduce prenatal exposure. Funding French Agency for Food, Environmental and Occupational Health & Safety, the EU's Horizon 2020 research and innovation programme, and the French Fund – Fondation de France. https://doi.org/10.1016/j.lanplh.2025.101330

Association of Urine Heavy Metals with Prevalence of Type 1 Diabetes and Poor Glycaemic Control,
Vasudevan, S. A., Seenivasan, S. N., Raghupathy, A. K., Vasudevan, D., Ayothi, P., Nayak, T., Gajendran, B., Durairaj, K., Sathish, D. S., Balaji, S., Kandasamy, A., Amaravathy, P., Mohanraj, S., Dhandapani, S., Pradeep, T., Swaminathan, K. and Velmurugan, G., *Biological Trace Element Research*, 2025.

Emerging evidence suggests that endocrine-disrupting chemicals specifically heavy metals, may influence metabolic disorders including Type 1 Diabetes mellitus (T1DM). Poor glycaemic control is a key issue in management of T1DM. This cross-sectional study explores the association of toxic heavy metals with prevalence of T1DM and glycaemia. A total of 153 individuals with T1DM with mean age of 13 years and age- and sex matched 60 healthy controls from Coimbatore, South India were recruited. Clinical data including glycated haemoglobin and sociodemographic and environmental exposure data were collected. Urine samples were analysed for Copper (Cu), Zinc (Zn), Cadmium (Cd), Arsenic (As), Barium (Ba) and Lead (Pb), which are all known endocrine-disrupting chemicals. Urinary concentrations of all heavy metals were normalized to urine creatinine and expressed as ug/mg creatinine. The levels of all analyzed metals were significantly higher in T1DM compared to controls. Correlation analysis revealed the positive association between glycaemia and heavy metals. Arsenic and lead showed significant trend with T1D prevalence on comparison to control while zinc and cadmium showed significant trend with uncontrolled glycaemia. This study reveals the association of heavy metals exposure on the etiology and pathophysiology of T1DM. In addition, this study highlights the need of screening of urinary heavy metals as part of metabolic risk assessment and development of targeted therapies for heavy metal detoxification for achieving better glycaemia in T1DM. https://doi.org/10.1007/s12011-025-04903-8

Reproductive toxicity of micro- and nanoplastics: Insights from experimental and human studies,
Wehrli, L., Martin, O. V., Trasande, L. and Damdimopoulou, P., *Journal of Internal Medicine*, Dec 2025, Vol. 298, no. 6, p. 532-561.

The exponential rise in plastic production has driven widespread contamination by micro- and nanoplastics (MNPs) in the environment. These plastic particles and their chemical additives have been detected in water sources, human bodily fluids, and reproductive tissues. With global fertility rates declining, their role as potential contributors is under investigation. This scoping review compares findings from in vitro experiments, in vivo studies across animal models, and epidemiological data to assess potential reproductive hazards associated with MNP exposure. Forty original studies published within the last decade were identified. MNPs have been detected in human breast milk, placenta, endometrium, ovaries, testis, semen, follicular fluid, blood, and urine samples. Humans are estimated to absorb 74,000-121,000 particles annually through inhalation, ingestion, skin contact, and use of plastic materials, including medical devices. Experimental evidence demonstrates that MNPs can cross biological barriers, interact with cells, and disrupt cellular pathways, including steroidogenesis, energy metabolism, inflammatory pathways, and

oxidative stress. Thirty in vivo animal studies have associated MNPs with altered reproductive endpoints in both males (i.e., altered semen quality and spermatogenesis) and females (i.e., altered folliculogenesis, depleted ovarian reserve, and reduced litter sizes), with possible transgenerational effects. In conclusion, current evidence suggests MNPs may represent a reproductive health hazard to humans and animals. The relative contributions of particle toxicity and their chemical additives remain difficult to disentangle. Overall, plastics and their associated chemicals represent a serious health and environmental concern, which continues to grow in the absence of restrictions and international agreements. https://doi.org/10.1111/joim.70038

The Effects of Trifluoroacetic Acid (TFA) in Humans: A Rapid Review,
Wipplinger, J., Meusburger, L., Dottolo, E., Galazka, S., Brunner, L., Füreder, A., Kundratitz, V., Rainer, K., Rauscher-Gabernig, E., Sarka, M. and Pleiner-Duxneuner, J., *Life (Basel)*, Nov 28 2025, Vol. 15, no. 12.

Human studies involving exposure to trifluoroacetic acid (TFA) and the associated clinical outcomes are typically not considered in standard chemical toxicity assessments. This review aimed to identify and synthesize all available human data on TFA exposure, regardless of study design or context. Given TFA's long-standing use and its formation as a degradation product of various compounds, a wide range of exposure scenarios was considered, including post-anesthesia monitoring, environmental assessments, and chemical incidents. The database searches in MEDLINE (PubMed) and EMBASE (Scopus) were conducted on 28 and 29 April 2025. A total of 17 studies met the inclusion criteria: 4 case reports, 3 case series, 5 observational studies, and 5 pharmacokinetic studies. All studies documented clear human exposure to TFA and reported at least one TFA-related outcome. Some acute exposures exceeded the currently proposed threshold values. However, no study demonstrated clinically relevant effects attributable to TFA. As a strong acid, TFA can cause typical corrosive injuries upon direct contact, but no additional systemic or organ-specific toxic effects were observed. https://doi.org/10.3390/life15121825

Association Between Mixed Exposure to Endocrine-Disrupting Chemicals and Cardiovascular Health: Results from the 2003-2016 NHANES,
Wu, D., Bing, S., Qiu, H., Wang, S. and Zhang, Y., *Cardiovasc Toxicol*, Dec 24 2025, Vol. 26, no. 1, p. 7.

Accumulating evidence supports the association between endocrine disrupting chemicals (EDCs) exposure and cardiovascular disease (CVD). However, the link between EDCs and cardiovascular health (CVH) prior to CVD onset remains unclear. This study investigates the relationship between individual and combined EDC exposure and Life's Essential 8 (LE8). We included 9,940 participants from the National Health and Nutrition Examination Survey (NHANES) conducted between 2003 and 2016, excluding adults with known CVD. Twenty-two types of EDCs were detected in urine samples, including three phenols, two phenolic pesticides, eleven phthalates, and six polycyclic aromatic hydrocarbons (PAHs). Weighted generalized linear models (GLM) and weighted quantile sum (WQS) regression to explore the relationship between single/mixed exposure to EDCs and CVH. Overall, 9,940 individuals (weighted mean [SE] age, 42.53 [0.26] years; 5,313 women [weighted 53.7%]) without CVD were included, with a mean score of LE8 at 68.70. The GLM model reveals that specific exposures to EDCs are inversely associated with LE8, serving as independent risk factors contributing to poorer CVH. The WQS index of EDCs was independently associated with overall CVH, with an adjusted odds ratio (OR) of 3.00 (95% confidence interval [CI]: 2.30-3.90; P < 0.001). 2-Fluorenone (2-FLU) emerged as the most heavily weighted component in the overall CVH model. This study emphasizes the association between exposure to EDCs is correlated with a higher odds ratio for decline in CVH among American adults. 2-FLU emerges as a prominent contributor. It provides

epidemiologic evidence for the detrimental effects of these chemicals on CVH.
https://doi.org/10.1007/s12012-025-10084-6

Associations of Paternal Seminal Plasma Metals with their Spouses' Unexplained Recurrent Spontaneous Abortion (URSA) Risk and the Potential Mediating Role of Oxidative Stress,
Xi, H., Yang, R., Bao, H., Li, H., Li, Y., Martin, F. L., Chen, W., Chen, L., Sun, Y., Lu, Y. Y., Huang, Q. and Tian, M., *Biol Trace Elem Res*, Dec 18 2025.

Unexplained recurrent spontaneous abortion (URSA) is a prevalent reproductive issue but its etiology remains obscure. Male exposure to environmental chemicals is suggested to elevate URSA risk in female partners. Herein, a case-control design set out to investigate associations between metal levels in human seminal plasma with URSA risk, plus to determine evidence of mediating effects by oxidative stress. Levels of 15 metal elements and oxidative stress marker malondialdehyde (MDA) in seminal plasma were measured in 125 male spouses of URSA cases compared to 108 male partners of women with successful pregnancy outcomes. The associations of single or mixed metals on URSA risk were analyzed using logistic regression and Bayesian kernel machine regression (BKMR), respectively. BKMR analyses reveal a joint effect of metal co-exposures on URSA risk. Through multiple statistical approaches, titanium (Ti), cadmium (Cd) or magnesium (Mg) were major contributors to metal mixtures elevating URSA risk. MDA was significantly and positively associated with URSA risk. Mediation analysis shows that the associations of Ti, Cd or Mg with URSA risk appear to be mediated by MDA at rates of 23.30%, 16.26% or 34.48%, respectively. In vitro experiments confirmed the seminal plasma relevant dose Ti, Cd or Mg exposure induced male mouse spermatocyte-derived GC-2 cells oxidative stress. Metal mixtures in seminal plasma are associated with increased URSA risk in female spouses, with Ti, Cd or Mg being significant contributors, potentially via oxidative stress, providing further insights into URSA etiology.
https://doi.org/10.1007/s12011-025-04949-8

PFAS Exposure and Endocrine Disruption Among Women,
Ripon, R. K., Hossain, M. J., Volquez, M., Meda-Monzon, E., Saunik, S. and Prasad, N., *JAMA Netw Open*, Dec 1 2025, Vol. 8, no. 12, p. e2539425.

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are commonly used in industrial and consumer products because of their heat resistance and hydrophobic and oleophobic properties.1 The primary sources of widespread PFAS exposure are contaminated drinking water, food, indoor dust, outdoor air, and soil.1 Nearly everyone in the US has detectable levels of PFAS in their blood.1 PFAS analytes can alter hormone secretion, menstrual cyclicity, and fertility and affect reproductive tissues directly or indirectly through endocrine disruption (ED).2 Despite increasing evidence associating single PFAS exposure with ED, a mixture of PFAS may hamper the association.3 However, there is limited evidence of the association of PFAS mixture exposure with ED. This study examines the association between single and mixture PFAS analytes exposure and ED among US women.
https://doi.org/10.1001/jamanetworkopen.2025.39425

Prenatal exposure to agricultural pesticide applications and gestational diabetes mellitus in the Az-PEARS population-based study (2014-2020),
Parra, K. L., Harris, R. B., Farland, L. V., Beamer, P., Fournier, A. J., Ellsworth, P. C. and Furlong, M., *Environ Int*, Dec 7 2025, Vol. 207, p. 109989.

BACKGROUND: Organophosphates (OP), pyrethroids (PYR), and carbamates (CAR) are pesticides widely-used for agricultural commercial purposes. Animal studies suggest that they may disrupt glucose metabolism during pregnancy. Few epidemiological studies have examined associations

between OP/PYR/CAR and gestational diabetes mellitus (GDM) risk, particularly during preconception (T0) and across pregnancy (Trimesters 1-3: T1-T3). METHODS: In this population-based study, we used Az-PEARS cohort, with 475,017 births from 2014 to 2020. Birth records were linked to Arizona's Pesticide Use Reports (PUR) to assess proximity to pesticide applications from maternal residence. Single pollutant models estimated associations between 3 pesticides classes, OP/PYR/CAR, and 18 active ingredients with GDM. Pesticide exposure within 500-meter buffer of the geocoded address of delivery was classified as any vs. none and log-transformed pounds applied. Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated using logistic-binomial regression, adjusting for maternal age, race/ethnicity, education, child sex, conception year, birth season, and T4. RESULTS: Several PYR pesticides were linked to GDM risk at T0 and T1, including beta-cyfluthrin (T1: RR = 1.18, 95 %CI: 1.06, 1.29), bifenthrin (T0: RR = 1.18, 95 %CI: 1.03, 1.34), cypermethrin (T0: RR = 2.13, 95 %CI: 1.61, 2.66), and permethrin (T0: RR = 1.17, 95 %CI: 1.10, 1.23). Additionally, OP exposure at T3 (RR = 1.11, 95 %CI: 1.02, 1.20) was associated with higher risk of GDM. Specifically, acephate, bensulide, dimethoate, and ethephon had positive associations ranging from RR = 1.11 to RR = 1.89. DISCUSSION: Exposure to pyrethroids in T0, and organophosphates in T3 are associated with higher GDM risk. Our findings suggest that critical windows of pesticide exposure may be important considerations for GDM risk.
https://doi.org/10.1016/j.envint.2025.109989

Toxicité sur l'homme

Perfluorooctanoic Acid (PFOA) and Perfluorooctanesulfonic Acid (PFOS),
IARC Monographs on the Identification of Carcinogenic Hazards to Humans Volume 135 (2025),

This volume of the IARC Monographs provides evaluations of the carcinogenicity of two agents, perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS), and their corresponding isomers and salts.
PFOA and PFOS are per- and polyfluoroalkyl substances (PFAS) that are extremely resistant to degradation. First produced in the 1940s, PFOA has extensive uses, including in fluoropolymer manufacture and applications; in surface coatings conferring stain-, oil-, and water-resistance on household products, carpets, textiles, leather products, and food and feed packaging; in electrics and electronics; and in construction materials. With some similar uses to those of PFOA, PFOS additionally has applications in aqueous film-forming foams used in firefighting; in the fabrication of imaging devices and semiconductors; in photolithography and electroplating; and in insulation, dyes, and ink. PFOA and PFOS occur ubiquitously in the environment, with high levels at pollution sources such as industrial sites and in firefighter-training areas and waste deposits. They may also be present in contaminated food, especially fish, seafood, and eggs. Occupationally exposed populations can have high levels of exposure, mainly via inhalation. The general population in contaminated areas is mainly exposed via drinking-water, and the general population in communities that are not near pollution sources is mainly exposed via diet and drinking-water.
An IARC Monographs Working Group reviewed evidence from epidemiological studies, cancer bioassays in experimental animals, and mechanistic studies to assess the carcinogenic hazard to humans of exposure to these agents and concluded that:
PFOA is carcinogenic to humans (Group 1);
PFOS is possibly carcinogenic to humans (Group 2B). https://publications.iarc.who.int/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Perfluorooctanoic-Acid-PFOA-And-Perfluorooctanesulfonic-Acid-PFOS--2025

The Threat of Micro-/Nanoplastics to Male Fertility: A Review of the Data and the Importance of Future Research,

Alex, S. A., George, N. K., Guardiola, J. and Clegg, D., *International Journal of Molecular Sciences*, Nov 26 2025, Vol. 26, no. 23.

Micro-/nanoplastics (MNPs) and their associated endocrine-disrupting chemicals (EDCs) have emerged as pervasive environmental pollutants, with growing concern for their impact on male reproductive health. In this review, we synthesize the findings from twenty-one peer-reviewed studies published between January 2019 and March 2025, selected through a structured literature search conducted in accordance with the SANRA guidelines. Emphasis was placed on studies examining the cellular effects of MNPs and EDCs on Germ, Leydig, and Sertoli cells. The literature indicates multiple mechanisms of testicular toxicity, including degradation of the blood testis barrier, disruption of signaling pathways critical for spermatogenesis and hormone synthesis, induction of oxidative stress and inflammation, and structural and genetic damage to testicular tissues. These data, primarily derived from in vitro and animal models, not only highlight significant biological disruptions but also underscore the limitations in extrapolating results to human physiology. Differences in exposure routes, dosages, and species-specific responses present challenges to direct translation to humans. This review concludes that further human-centric research that mimics real-life exposure and impacts is essential to assess chronic, low-dose exposures and bridge the gap between experimental data and real-world reproductive outcomes, ultimately informing public health strategies and guiding future investigations into the reproductive risks posed by MNPs and EDCs. https://doi.org/10.3390/ijms262311457

The hidden health effects of endocrine-disrupting chemicals,
Alonso-Magdalena, P., *Nat Rev Endocrinol*, Feb 2026, Vol. 22, no. 2, p. 70-71.

The quest to understand the adverse health outcomes linked to endocrine-disrupting chemicals continued in 2025. Insights have been gained regarding their effects on metabolic health, their key characteristics, the mechanisms underlying their effects and the burden of disorders associated with exposure to these chemicals in terms of mortality and life-years lost.
https://doi.org/10.1038/s41574-025-01222-9

Analysis of bisphenol A-modulated expression of hypothalamic thyroid, estrogen, and peroxisome proliferator-activated receptors and concurrent mitochondrial dynamics following short-term exposure in mice,
Alymbaeva, D., Zsarnovszky, A., Szabo, C., Kiss, D. S., Bartha, T. and Jocsak, G., *Current Research in Toxicology*, 2025 2025, Vol. 9.

Endocrine-disrupting chemicals (EDCs) represent a significant and growing threat to human and animal health, exerting tissue- and concentration-specific effects on endocrine function. This study investigated the acute impact of bisphenol A (BPA) on nuclear receptor signaling and mitochondrial dynamics in hypothalamic AgRP-NPY (agouti-related peptide; neuropeptide Y) and POMC (pro-opiomelanocortin) neurons. Mice received a single intraperitoneal injection of BPA at doses of 40 mu g/kg, 5 mg/kg, or 10 mg/kg, and were assessed 6 h postexposure. Quantitative analysis of hypothalamic mRNA expression revealed that low-dose BPA (40 mu g/kg) didn't affect ER alpha (estrogen receptor alpha), TR alpha (thyroid receptor alpha), but significantly upregulated PPAR gamma (peroxisome proliferator-activated receptor gamma). Concurrently, mitochondrial respiration and ultrastructure exhibited dose-dependent alterations, with diminished effects observed at higher BPA concentrations. These findings demonstrate that BPA elicits rapid, dose-dependent modulation of nuclear receptor gene expression and mitochondrial dynamics in hypothalamic neurons. The data suggest mitochondria serve as early subcellular targets of EDC

exposure. This underscores the importance of evaluating low-dose EDC effects to improve risk assessment and regulatory frameworks. https://doi.org/10.1016/j.crtox.2025.100263

Pharmacokinetics and Pharmacodynamics of Perfluorooctane Sulfonate (PFOS) and Its Role in the Development and Progression of Prostate, Ovarian and Breast Cancers,
Arunsi, U. O., Ezirim, D. C., Arunsi, C. C., Altayyar, A., Uche, E. G., Jonathan, F. C., Opieh, A. K., Anadi, I. V., Ofoegbu, C. O., Nwankwo, V. C., Ugbogu, E. A., Etusim, P. E. and Owumi, S., *Cancers*, Oct 31 2025, Vol. 17, no. 21.

Environmental pollution, driven by industrialization, urbanization, and agricultural practices, has intensified global ecological degradation. Among the most concerning pollutants is PFOS, a synthetic compound known for its chemical stability, environmental persistence, and bioaccumulative potential. Widely utilised in industrial and consumer products, PFOS infiltrates ecosystems and food chains, posing substantial risks to human and animal health. Upon exposure, PFOS disrupts lipid metabolism, damages cellular membranes, and alters signaling pathways through partial metabolism by cytochrome P450 enzymes. Accumulating evidence links PFOS to oxidative stress, mitochondrial dysfunction, endocrine disruption, neurotoxicity, and immunotoxicity. Critically, PFOS contributes to the development and progression of prostate, breast, and ovarian cancers via mechanisms such as hormonal interference, chronic inflammation, and epigenetic modifications. Epidemiological studies further associate elevated PFOS serum levels with increased cancer risk, particularly in occupationally and environmentally exposed populations. This review brings together the latest knowledge on PFOS emissions, mechanistic toxicity, and cancer-causing potential, highlighting the urgent need for focused research and improved regulatory measures to safeguard public health. https://doi.org/10.3390/cancers17213507

Perfluorodecanoic acid (PFDA) induces oxidative stress and autophagy dysregulation in HGrC1 cells,
Barakat, R. A., Lee, C., Ball, H. B. and Clark, K. L., *Reproductive Toxicology*, Mar 2026, Vol. 140.

Perfluorodecanoic acid (PFDA), a long-chain per- and polyfluoroalkyl substance (PFAS), is an emerging environmental toxicant, though little is known on its impact on female reproduction. This study investigates the cellular effects of PFDA on a human granulosa cell line, HGrC1, focusing on oxidative stress and autophagy pathways. HGrC1 cells were exposed to increasing concentrations (0.01 - 10 mu M) of PFDA for 24, 48, 72, and 96 h. Notably, 10 mu M PFDA for 48 h resulted in approximately 50 % reduction in cell viability, activation of cleaved caspase-3, reduced cell density, and altered morphology characterized by spindle-shaped elongation. qRT-PCR revealed significant downregulation of key antioxidant genes, particularly catalase. PFDA exposure markedly increased intracellular reactive oxygen species levels. Western blot analysis of the p62-Keap1-Nrf2 signaling pathway showed decreased KEAP1 protein levels and strong nuclear accumulation of NRF2 at 10 mu M PFDA, supported by elevated expression of the downstream target HO-1. In parallel, PFDA disrupted autophagy regulation. Accumulation of p62, along with increased levels of LC3A/B, suggested impaired autophagic flux. Together, these findings demonstrate that PFDA compromises granulosa cell survival by inducing oxidative stress, altering antioxidant gene expression, and dysregulating autophagy. Given the central role of granulosa cells in follicular development and hormone synthesis, PFDA-induced toxicity may have significant implications for ovarian function and female fertility. https://doi.org/10.1016/j.reprotox.2025.109136

A Review of the Potential Endocrine Bioactivity of 2-Ethylhexyl 4-Hydroxybenzoate (2-EHHB),
Bever, R. J., Fallacara, D. M., Hamernik, K., Kamel, A., Lynn, S. G., Irwin, W. and Matten, S., *J Appl Toxicol*, Dec 12 2025.

Available data, including results from six in vivo studies conducted by the United States (US) Environmental Protection Agency (EPA) were reviewed to assess the potential of 2-ethylhexyl 4-hydroxybenzoate (2-EHHB) to affect endocrine pathways. 2-EHHB is a paraben, and parabens are used in the cosmetics, food, and pharmaceutical industries. It was selected for testing based on in vitro bioactivity scores from androgen receptor (AR) and estrogen receptor (ER) pathway models provided in the US EPA Computational Toxicology Chemicals Dashboard. The following assays were performed using US EPA Endocrine Disruptor Screening Program (EDSP) Tier 1 and Tier 2 test guidelines: Hershberger, male pubertal, amphibian metamorphosis assay (AMA), fish short-term reproduction assay (FSTRA; medaka, fathead minnow, and zebrafish), larval amphibian growth and development assay (LAGDA), and medaka extended one-generation reproduction test (MEOGRT). Published data from uterotrophic assays performed in Japan were also reviewed. Based on this evaluation, estrogen agonism was the best supported mechanism of action and there was no clear support for thyroid hormone perturbation. Among the in vivo assays reviewed, the Japanese medaka and African clawed frog were the most sensitive test species. Results from the MEOGRT indicated decreased fecundity (all generations) at concentrations ≥ 5.32 µg/L. Decreased fecundity and fertilization at ≥ 10.6 µg/L in the medaka FSTRA support those results. LAGDA results indicated delayed development at ≥ 5.33 µg/L, but the mechanism was unclear based on the available data. https://doi.org/10.1002/jat.70020

The nexus of environmental endocrine-disrupting chemical exposure and metabolic dysfunction-associated steatotic liver disease: An emerging public health challenge,
Chen, H. X., Cui, H. and Meng, Z. J., *Ecotoxicology and Environmental Safety*, Jan 1 2026, Vol. 309.

The global prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) has reached epidemic proportions, creating a substantial healthcare burden. While traditionally attributed to caloric excess and sedentary lifestyles, the incomplete explanation provided by these factors alone has spurred the investigation of novel etiological agents. There is now compelling evidence that chronic, low-dose exposure to environmental endocrine-disrupting chemicals (EDCs) is a significant and underappreciated risk factor driving MASLD pathogenesis. This review synthesizes the current human epidemiological and mechanistic evidence, focusing on the last five years, to elucidate the role of both established EDCs (e.g., phthalates, bisphenols, PFAS, organochlorine pesticides) and emerging contaminants, notably micro- and nanoplastics (MNPs). We detail how these pervasive pollutants promote hepatic steatosis, inflammation, and fibrosis by disrupting nuclear receptor signaling (e.g., PPAR gamma), inducing gut dysbiosis and barrier dysfunction, causing mitochondrial and lysosomal impairment, and reprogramming lipid metabolism. The review highlights that MNPs, in particular, represent a frontier in environmental hepatotoxicity, with recent data revealing their ability to bioaccumulate and exacerbate metabolic insults through novel mechanisms. By integrating evidence from population studies and experimental models, this review underscores the necessity of incorporating the "exposome" into the MASLD etiological framework. It concludes that mitigating this public health challenge requires concerted efforts in advancing research on chemical mixtures and critical exposure windows, alongside implementing policies aimed at reducing environmental exposure. https://doi.org/10.1016/j.ecoenv.2025.119513

Effets non reprotoxiques des perturbateurs endocriniens,
Chevalier, N., Hinault-Boyer, C. and Magnifico, S., *Actualités Pharmaceutiques*, 2026/01/01/ 2026, Vol. 65, no. 652, p. 32-37.

Les perturbateurs endocriniens sont capables d'interférer avec les systèmes de régulation hormonale et de nuire à notre santé. Les données de la littérature sont assez fournies quant

aux pathologies gonadiques mais ces dernières années ont permis de mettre en évidence leur impact néfaste sur l'ensemble des autres systèmes endocrines (diabète, obésité, thyroïde) et ses conséquences sur le développement neurocognitif. La liste risque de ne pas se limiter à ces seules entités, il est donc primordial que les professionnels de santé adressent des messages clairs à leurs patients de manière à limiter leur exposition et ainsi espérer diminuer les effets néfastes de ces molécules à court et long termes. Non-reprotoxic effects of endocrine disruptors Endocrine disruptors can interfere with hormonal regulation systems and harm our health. The literature provides ample data on gonadal disorders, but in recent years, their harmful impact on all other endocrine systems (diabetes, obesity, thyroid) and their consequences on neurocognitive development have been highlighted. The list may not be limited to these entities alone, so it is essential that healthcare professionals send clear messages to their patients in order to limit their exposure and thus hopefully reduce the harmful effects of these molecules in the short and long term. https://doi.org/10.1016/j.actpha.2025.10.013

What Is the Impact of Glyphosate on the Thyroid? An Updated Review,
Choudhary, L., Monaghan, M., Schweppe, R., Franco, A. T., Goldner, W. and Van Gerwen, M., *Biomedicines*, Sep 30 2025, Vol. 13, no. 10.

Background/Objectives: Thyroid dysfunction (hypo- and hyperthyroidism) and cancer incidence have increased over the past decades, possibly linked to environmental contributions from endocrine disrupting chemicals (EDCs). Glyphosate is one of the most widely used herbicides globally and has endocrine-disruptive properties. Because of the sensitivity of the thyroid gland to endocrine disruption and the increased glyphosate exposure worldwide, this comprehensive review aimed to summarize studies investigating the link between glyphosate/glyphosate-based herbicides (GBHs) and thyroid dysfunction in human, animal, and in vitro studies. Methods: PubMed, Scopus, and Embase were used to search for original studies assessing glyphosate or GBH exposure and thyroid-related outcomes through December 2024. Data were extracted on study design, population or model, exposure, and thyroid outcomes. A total of 28 studies, including 9 human, 3 in vitro, and 16 animal studies were included. Results: Human studies showed mixed findings with some suggesting associations between glyphosate exposure and altered thyroid hormone levels, while others found no significant effects. Animal studies, particularly in rodents and amphibians, showed thyroid hormone disruption and altered gene expression, especially after perinatal or developmental exposure. In vitro studies reported changes in thyroid-related gene transcription and cell viability, however at concentrations exceeding those seen in humans. Conclusions: While there is some evidence that glyphosate may disrupt thyroid function, differences in study populations, exposure assessment methods, species models, and exposure doses complicated the comparison and summarization of the results. Further mechanistic and longitudinal studies are needed to clarify the thyroid-specific risks of glyphosate exposure. https://doi.org/10.3390/biomedicines13102402

Bisphenol A triggers adipocyte dysfunction, thereby fostering triple-negative breast cancer aggressiveness,
Citarella, A., Autilio, T. M., Besharat, Z. M., Vicentini, E., Barbagallo, F., Splendiani, E., Di Fiore, A., Venneri, M. A., De Smaele, E., Catanzaro, G., Masuelli, L., Bei, R. B. R., Fabi, A., Mardente, S., Angeloni, A., Migliaccio, S., Po, A. G. S. and Ferretti, E., *Environmental Research*, Feb 1 2026, Vol. 290.

Bisphenol A (BPA) is an organic compound widely used in the production of polycarbonate plastics and epoxy resins. As a pervasive environmental pollutant, BPA accumulates in adipose tissue (AT) due to its lipophilic properties. AT, an endocrine organ central to homeostasis, constitutes the main component of breast stroma and plays a pivotal role in the microenvironment of breast cancer,

including triple-negative breast cancer (TNBC). This study investigated how BPA disrupts adipocyte differentiation and metabolism, and the subsequent effects on the crosstalk between adipocytes and TNBC cells. We induced adipogenic differentiation of preadipocytes in the presence of BPA and evaluated alterations in differentiation and cytokine secretion. TNBC cells were cultured in homotypic and heterotypic organoids, exposing them to BPA either directly or indirectly, through a conditioned medium of BPA-treated adipocytes. BPA exposure altered adipocyte differentiation, reducing lipid accumulation and perturbing cytokines release, leading to the upregulation of molecules involved in cell migration and invasiveness. TNBC cells exposed to conditioned medium of BPA-treated adipocytes exhibited enhanced growth, migration and invasiveness, whereas direct BPA treatment did not induce significant changes. These indirect effects were, at least in part, mediated by SDF1 alpha and GAS1. Moreover, TNBC organoids showed increased infiltrative capacity when co-cultured with BPAconditioned adipocytes. These findings highlight the profound impact of environmental pollution on cancer progression. BPA perturbates adipose differentiation, creating a dysfunctional adipocyte that fosters cancer growth and invasiveness in TNBC. This study underscores the impact of environmental pollutants on tumour progression by revealing the importance of BPA perturbation on tissue homeostasis and how this could promote cancer.
https://doi.org/10.1016/j.envres.2025.123446

Endocrine-disrupting effects of environmental BPS and PFOS on human brain organoid development,
Di Credico, A., Gaggi, G., Bibbò, S., Blenkinsop, T. A., Di Baldassarre, A. and Ghinassi, B., *Frontiers in Endocrinology*, Dec 4 2025, Vol. 16.

Objective Prenatal exposure to environmental endocrine-disrupting chemicals (EDCs) has been increasingly linked to neurodevelopmental impairment. Bisphenol S (BPS) and perfluoro-octane sulfonate (PFOS), two widely distributed EDCs detected in maternal and fetal tissues, raise concern due to their potential to interfere with brain development even at low environmental doses.Methods a phenotypic screening on human iPSC-derived cerebral organoids was performed to explore whether chronic exposure to BPS and PFOS could affect key neurodevelopmental processes.Results Both compounds affected key neurodevelopmental processes, including neuronal proliferation, cortical specification, synaptogenesis, glutamatergic differentiation, mitochondrial function, and choroid plexus formation. Importantly, TUNEL assay confirmed the absence of significant cytotoxicity. BPS exposure was associated with reduced ER beta, GPER, and phosphorylated Akt expression, suggesting a possible involvement of estrogen-related pathways. PFOS exposure coincided with decreased transthyretin expression, suggesting a potential influence on thyroid hormone availability.Conclusions Exposure to multiple EDCs may disrupt distinct endocrine axes, producing cumulative impacts on human brain development. These findings underscore the value of human-relevant models for identifying endocrine-mediated neurodevelopmental hazards. While the observed molecular changes suggest distinct hormonal pathways may be involved, future mechanistic studies, including co-exposures with receptor modulators, will be required to establish causal relationships.
https://doi.org/10.3389/fendo.2025.1692333

Environmental pollutants as emerging risk factors in osteoarthritis: Mechanistic and epidemiological evidence,
Duan, H. M., Liang, F., Deng, L., Liu, S. M., Ren, Z. Z. and Li, J. W., *Ecotoxicology and Environmental Safety*, Jan 1 2026, Vol. 309.

Osteoarthritis (OA) is a multifactorial degenerative joint disease with increasing evidence implicating environmental pollutants as underrecognized contributors to its pathogenesis. This

review Edited by Dr. Caterina Faggiostematically synthesizes in vitro, animal, computational, and human epidemiological studies to elucidate the mechanistic and population-level effects of chemical exposures on OA. Airborne pollutants, including PM2.5, PM10, NO2, O3, and trihalomethanes, are associated with increased OA incidence, promoting cartilage degradation through oxidative stress, inflammatory cytokine overproduction, and epigenetic or developmental programming. Heavy metals such as cadmium, lead, arsenic, mercury, and copper induce reactive oxygen species (ROS), chondrocyte apoptosis, extracellular matrix (ECM) breakdown, and systemic inflammation, with both experimental and epidemiological studies demonstrating dose-dependent relationships. Persistent organic pollutants, including polychlorinated biphenyls (PCBs) and per-/polyfluoroalkyl substances (PFAS), disrupt autophagy, endocrine signaling, and cartilage homeostasis, with evidence of bioaccumulation in synovial fluid and modulation of gene expression relevant to bone-cartilage metabolism. Endocrine-disrupting chemicals, including phthalates, brominated flame retardants, and acetyl tributyl citrate, further exacerbate OA susceptibility via MAPK and NF-kappa B pathway activation, ROS generation, and ECM dysregulation. Epidemiological data consistently demonstrate associations between these exposures and OA prevalence, incidence, and symptom severity, often showing additive or synergistic effects for multiple pollutants. Despite these advances, research is limited by cross-sectional designs, high-dose experimental models, incomplete assessment of pollutant mixtures, and geographic and joint-specific biases. Future studies should prioritize longitudinal cohort designs, repeated biomonitoring, mechanistic exploration of mixture effects, and inclusion of emerging pollutants such as microplastics. Integrating environmental exposure assessment with advanced imaging, omics technologies, and computational modeling will enhance understanding of pollutant-induced OA mechanisms. Collectively, this evidence underscores the need for environmental interventions, public health strategies, and preventive approaches aimed at mitigating pollutant-driven joint degeneration, highlighting environmental exposures as a critical, yet modifiable, determinant of OA risk. https://doi.org/10.1016/j.ecoenv.2025.119453

Evaluating the Endocrine-Disrupting and Oxidative Stress Potential of a 50-Component Human-Relevant Complex Chemical Mixture Using In Vitro Tests,
Engelhardt, J., Struwe, N., Jansson, A., Kos, V., Larsson, M. and Weiss, J., *Journal of Applied Toxicology*, 2025.

Humans are chronically exposed to mixtures of environmental contaminants. Exposure to endocrine-disrupting chemicals (EDCs) contributes to increased health impairment observed globally. This study aimed to evaluate the endocrine-disruptive and oxidative stress potential of a human-relevant, complex chemical mixture in vitro. By testing chemical class subgroup mixtures, the identity of toxicological drivers and mixture additivity could be investigated. A 50-component mixture was compiled based on Swedish human blood concentrations (xHBC), consisting of six subgroup mixtures: polychlorinated biphenyls (PCBs) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (PCB mixture), brominated flame retardants (BFR mixture), per- and polyfluoroalkyl substances (PFAS mixture), pesticide mixture, synthetic phenolic contaminants (phenol mixture), and phthalate mixture. These were tested in four chemically activated luciferase gene expression (CALUX) assays: dioxin responsive (DR-), estrogen receptor alpha (ER alpha-), androgen receptor. (AR-), and nuclear factor erythroid 2-related factor 2 (Nrf2)-CALUX, along with an adipocyte cell assay. The total mixture caused significant agonistic activity in DR- and ER-, and antagonistic activity in AR-CALUX at 0.1-15 xHBC, depending on the assay. Mixture additivity was assessed in ER alpha-, DR-, and anti-AR-CALUX using subgroup mixtures and the concentration addition (CA) model. The total mixture followed the CA model in ER alpha-, anti-AR- and DR-CALUX. The toxicological drivers of these activities were mainly the PCB and phenol mixture. A significant increase in differentiated adipocytes was observed at 100 xHBC. These results raise concerns regarding potential health effects on the endocrine system. The additive effects at human-relevant concentrations observed in

this study motivate considering mixtures in regulatory contexts to protect the well-being of future generations. https://doi.org/10.1002/jat.70011

Impact of bisphenol A exposure on fetal brain development and neurological health-a review, Feng, J., Mazari, M. E., Yasmin, S., Riaz, A., Uddin, J., Hussain, A. I., Masood, F. Z., Zhong, J. X. and Kamal, G. M., *Environmental Science-Advances*, 2025.

Bisphenol A (BPA), a ubiquitous industrial material, is widely employed as a starting material in preparing epoxy resins and polycarbonate plastics. This compound is utilized on a very large scale around the globe. As this compound has been classified as one of the EDCs, substantial evidence has demonstrated a positive correlation between BPA exposure and developmental disorders in the fetal central nervous system as well as fetal neurodevelopment. Its exposure also affects memory formation and the normal functioning of the pituitary gland. Bisphenol has adverse effects on thyroxine, alternatively affecting fetal physical development. BPA also affects sexual behaviors and causes hypersexuality. In addition, BPA exposure leads to certain epigenetic and transgenerational effects. The main aim of our review is to highlight the impact of BPA on fetal neurodevelopment and mental behavior. It is essential to completely understand the mechanism of action of BPA on the molecular structure of interneurons and other neurons during fetal development due to BPA exposure. This will help in the evaluation of interneuron linkage and other neural activities along with brain development from the fetal stage to mature life. This review encompasses the literature available on the abnormal impacts of BPA on fetal development due to maternal exposure to BPA. We have surveyed the relevant literature to disseminate the information obtained through research carried out to reveal these impacts. https://doi.org/10.1039/d5va00145e

Interaction-profile cheminformatic read-across identifies the UV filter benzophenone-4 as a PPARγ agonist and potential obesogen,
Gong, J., Park, I. G., Hwang, S., Cho, J., Lee, M. J., Kim, M., Kang, J., An, S. and Noh, M., *Toxicology*, Feb 2026, Vol. 520.

Obesogens are chemicals, often encountered as environmental contaminants, that disrupt metabolic regulation and promote obesity. Here, we present a cheminformatics framework that integrates interaction-profile docking simulations with cluster-level enrichment analysis to enhance read-across and prioritize candidate environmental metabolic disruptors. Protein-ligand contact features from docking to obesity-related nuclear receptors were summarized at the pose level and combined into a 327-dimensional interaction-profile descriptor. Dimensionality-reduced descriptors from 6022 Tox21 compounds were clustered, and enrichment analysis against Tox21 assay results identified clusters associated with specific nuclear receptor activities. One cluster was selectively enriched for peroxisome proliferator-activated receptor gamma (PPAR gamma) agonists. Although benzophenone4 (BP-4, sulisobenzone), a sunscreen UV filter in this cluster, is labeled as inactive in Tox21, experimental validation confirmed selective PPAR gamma binding and recruitment of SRC-2 and PGC-1 alpha coactivators. In human bone marrow-derived mesenchymal stem cells, BP-4 promoted adipogenic differentiation, lipid accumulation, and adiponectin production, establishing its potential as an environmental obesogen. This study demonstrates the power of combining interaction-profile read-across with functional assays to predict environmental metabolic disruptors and provides a mechanistic template for systematic chemical safety evaluation. https://doi.org/10.1016/j.tox.2025.154362

A Review of the Literature on the Endocrine Disruptor Activity Testing of Bisphenols in Caenorhabditis elegans,

Hockicková, P., Kaiglová, A., Korabečná, M. and Kucharíková, S., *Journal of Xenobiotics*, 2026, Vol. 16, no. 1, p. 7. https://www.mdpi.com/2039-4713/16/1/7

Endocrine disruptors, immune dysregulation, and Alzheimer's disease: A multi-omics approach to uncovering environmental neurogenetics,
Hong, Y. G., *Environmental Chemistry and Ecotoxicology*, 2025 2025, Vol. 7, p. 2631-2642.

Alzheimer's disease (AD) is a progressive neurodegenerative disorder influenced by both genetic and environmental factors. Endocrine-disrupting chemicals (EDCs), which are widely present in consumer products and industrial waste, have been implicated in neurotoxicity, but their causal role in AD remains unclear. In this study, we integrated chemical-gene interaction data, blood-based cis-eQTLs, and genome-wide association study (GWAS) summary statistics to investigate whether EDC-regulated gene expression is causally linked to AD risk. Using Mendelian randomization (MR) and Bayesian colocalization analyses, we identified 27 genes with significant associations, among which 12 genes, including CCNE2, SEMA4G, and NDUFS2, showed strong evidence of colocalization with AD risk loci. Enrichment analyses revealed that these genes are involved in immune regulation and mitochondrial function, particularly natural killer (NK) cell cytotoxicity and mitochondrial ribosomal pathways. Single-cell RNA sequencing of peripheral blood mononuclear cells further demonstrated that colocalized genes were differentially expressed in specific immune cell subsets in AD patients, particularly NK and T cells. Our findings provide genetic evidence that EDCs may influence AD pathogenesis through immune and mitochondrial dysregulation. This study highlights the importance of environmental factors in AD and offers novel insights into molecular targets for prevention and therapeutic development. https://doi.org/10.1016/j.enceco.2025.10.023

Exposition aux PFAS pendant la grossesse. Conséquences sur la santé et le fonctionnement du placenta,
Khan, S., Ouidir, M., Alfaidy, N. and Philippat, C., *Med Sci (Paris)*, Nov 2025, Vol. 41, no. 11, p. 837-839.

Le placenta assure les échanges de nutriments et de gaz entre la mère et le fœtus, ainsi que les fonctions endocriniennes et métaboliques nécessaires au bon déroulement de la grossesse. Le poids du placenta ainsi que le rapport entre celui-ci et le poids fœtal sont couramment utilisés comme indicateurs de la santé et de l'efficacité du placenta. Bien que moins fréquemment exploitée dans les études épidémiologiques en raison de contraintes techniques, sa structure microscopique constitue également un indicateur essentiel : l'analyse histologique du placenta fournit en effet des informations précieuses sur la perfusion vasculaire, les échanges avec le fœtus, ainsi que sur son degré de « vieillissement ». Une altération du poids du placenta ou de ses caractéristiques histologiques est associée à des complications majeures de la grossesse, telles que la prééclampsie1, le retard de croissance intra-utérin ou la naissance prématurée. Ces éléments justifient l'intérêt porté à ces marqueurs dans l'étude de l'impact des contaminants environnementaux sur l'issue de la grossesse et la santé périnatale. https://doi.org/10.1051/medsci/2025210

Adverse effects of halogenated organic compounds on implantation and placental development,
Kim, M., Song, G. and Park, S., *Molecular & Cellular Toxicology*, 2025.

Purpose of reviewThis review summarizes experimental models of female reproductive systems and pregnancy, providing insights into the toxic mechanisms of halogenated organic compounds (HOCs). We elucidated the physiological effects of HOCs on pregnancy focusing on their adverse effects on implantation and placental formation.Recent findingsHOCs defined as organic compounds containing halogen atoms such as fluorine, chlorine, and bromine, have been widely used in various

industrial fields. Due to their high lipid affinity, cell membrane permeability, and environmental persistence, HOCs are likely to accumulate in biological systems. As a result, HOCs are considered important issues from the perspective of environmental toxicity, as they can induce continuous adverse effects on the female reproductive system, particularly during implantation and placentation. Implantation and placental formation are delicately controlled by the complex interaction of the trophoblast, uterine endometrial cells, and maternal immune systems. The previous studies were reported that HOCs disrupt immune modulation, hormonal responses, and interactions between trophoblast and endometrium cells, leading to implantation failure and placental dysfunction. Based on these findings, this review discusses current experimental models and mechanistic insights into HOCs-induced female reproductive toxicity. Through this, we suggest a research direction for improving risk assessment of HOCs and managing environmental hazards.
https://doi.org/10.1007/s13273-025-00591-6

Microplastics, Endocrine Disruptors, and Oxidative Stress: Mechanisms and Health Implications, Kovacs, K., Bodis, J. and Vass, R. A., *International Journal of Molecular Sciences*, 2026, Vol. 27, no. 1, p. 399.

Microplastics and nanoplastics (<5 mm and <1 µm, respectively) are emerging contaminants now ubiquitous across environmental matrices and increasingly recognized for their impacts on human health. These particles commonly adsorb or contain endocrine-disrupting chemicals—such as bisphenol-A and phthalate additives—that together trigger complex biological responses. This review examines the central role of oxidative stress in mediating the toxicity of microplastics and associated endocrine disruptors across multiple organ systems. We discuss mechanisms including cellular uptake, reactive oxygen species generation, mitochondrial dysfunction, impairment of antioxidant defenses, and activation of key signaling pathways. Organ-specific effects on reproductive health, cardiovascular function, hepatic metabolism, gut barrier integrity, and neurological systems are highlighted. Current evidence strongly supports oxidative stress as a pivotal mechanism linking microplastic exposure to systemic toxicity, underscoring important implications for public health policy and clinical intervention strategies. https://doi.org/,
https://www.mdpi.com/1422-0067/27/1/399

Interplay between aryl hydrocarbon and estrogen receptor signaling- A possible explanation of endocrine- disrupting and immunomodulatory effects of mycotoxins,
Kowalska, K., Elesh, I. F. I. and Marko, D., *Journal of Hazardous Materials*, 2026/01/01/ 2026, Vol. 501, p. 140838.

Although the endocrine-disrupting (ED) and immunomodulatory effects of mycotoxins are well documented, both in vitro and in vivo, little is known about their detailed molecular mechanisms. Here, we elucidated two known effects of mycotoxins: ED and immunomodulatory, and proposed the possible linker: the interplay between aryl hydrocarbon receptor (AhR) and estrogen receptor (ER) signaling pathways. We reviewed in detail the immunomodulatory role of both AhR and ER signaling pathways and suggested their possible interaction, which might result in ED and immunomodulatory effects. This research may serve as a future direction for both mycotoxin and other environmental toxin research, paving the way for comprehensive mechanistic insights that link risk assessment, toxicology, and molecular biology.
https://doi.org/10.1016/j.jhazmat.2025.140838

The effects of house dust-derived mixtures of organophosphate esters on Leydig cell phenotype, function, and lipidome†,

Li, Z. X., Wang, X. T., Hales, B. F. and Robaire, B., *Biology of Reproduction*, Dec 2025, Vol. 113, no. 6, p. 1587-1600.

Organophosphate esters (OPEs), widely used as flame retardants and plasticizers, are frequently detected in indoor environments and human tissues, raising concerns about their potential endocrine-disrupting effects. In this study, we examined the effects of a household dust-based mixture of OPEs, along with two structural distinct sub-mixtures, on the phenotype, function, and lipidome on MA10 Leydig cells. Using high-content imaging, we identified increase in oxidative stress levels and accumulation of lipid droplets as common phenotypic effects across mixtures. Notably, the triaryl OPE sub-mixture exhibited greater potency, suggesting that specific structural features contribute to the toxicity of OPEs. While the OPE mixture did not impair basal steroid hormone production in MA-10 cells, changes were observed in stimulated progesterone levels and transcriptional regulation of key steroidogenic transcripts. When comparing lipidomic profiles across three steroidogenic cell lines (MA-10, H295R, and KGN), we found that glycerolipids, particularly triglycerides and diglycerides, consistently appeared to be the most affected lipid species, highlighting a common disruption in the composition of lipid droplet. However, cell line specific effects were also observed, especially in the regulation of cholesterol esters, likely reflecting differences in cholesterol sourcing and steroidogenic pathways. These findings emphasize the importance of evaluating environmentally relevant chemical mixtures and demonstrate that OPEs can disrupt steroidogenic function and lipid metabolism.Sentence Environmentally relevant OPE mixture affects the phenotype, function, and lipidome of MA-10 Leydig cells, with the triaryl OPE component showing higher toxicity in inducing oxidative stress and lipid droplet accumulation. https://doi.org/10.1093/biolre/ioaf229

Unraveling the Mechanisms of Osteoporosis Triggered by Methylparaben and Monomethyl Phthalate through Integrated Mendelian Randomization, In Silico Simulations, and Experimental Validation,
Liu, H., Xu, X., Du, L., Zhang, W., Guo, Y., Zhang, F., Sun, H., Si, H. and Liu, P., *Environ Sci Technol*, Dec 17 2025.

Endocrine-disrupting chemicals (EDCs) are pervasive environmental hazards that have been linked to osteoporosis (OP), though causal mechanisms remain elusive. Employing an integrated multiomics framework, this study combined bidirectional Mendelian randomization (MR), network toxicology, machine learning, molecular simulations, and ovariectomized rat models to elucidate causal relationships between EDCs and osteoporosis, and to identify the molecular underpinnings of these relationships. MR analyses leveraging European GWAS data identified methylparaben (MP; OR = 0.973, p < 0.001) and monomethyl phthalate (MMP; OR = 0.984, p = 0.006) as causal agents reducing bone mineral density (BMD), validated across two independent cohorts. Network toxicology revealed CYP3A4 as a shared target for both EDCs, with HSPA5-driven endoplasmic reticulum (ER) stress implicated in MP-induced bone loss and CRP-mediated inflammation central to MMP pathology. Molecular dynamics simulations confirmed stable binding of MP/MMP with hub targets. Crucially, ribosomal genes (RPL9/RPL37A/RPS19) altered by MP were mechanistically linked to ER stress-induced osteotoxicity rather than direct EDC binding. In vivo validation demonstrated that MP and MMP exposure in OVX rats significantly exacerbated trabecular degradation, suppressed osteogenic markers, and elevated osteoclastic activity. This work establishes CYP3A4 as a high-value therapeutic target for countering EDC-induced osteoporosis and resolves longstanding controversies regarding the osteotoxic mechanisms of parabens and phthalates. https://doi.org/10.1021/acs.est.5c12267

Phthalates exposure as a risk factor for gestational diabetes mellitus: Integrated evidence from epidemiological and human liver organoids studies,
Liu, H. H., Yang, Z. J., Tian, Y. R., Zhuang, Z. S., Shi, M. Y., Cui, H. Y., Ji, X. N., Wang, Y. X., Wang, X. H., Zhao, X. B., Jia, X. D., Wan, Y., Yang, H. and Yu, S. J., *Ecotoxicology and Environmental Safety*, Nov 1 2025, Vol. 306.

Gestational diabetes mellitus (GDM) poses significant risks to both maternal and child health, and its rising incidence necessitates exploration of environmental risk factors. In GDM development, the role of environmental risk factors such as phthalates, a ubiquitous class of endocrine-disrupting chemicals, is not well understood. In this study, we integrated epidemiological and toxicological studies to explore the association between phthalates exposure and GDM risk. We detected ten major phthalates metabolites in serum samples from a GDM casecontrol cohort and found that the levels of Monobutyl phthalate (MBP), Monoethylhexyl phthalate (MEHP), Monoethyl phthalate (MEP), and Monobenzyl phthalate (MBzP) were significantly elevated in GDM patients compared to healthy controls. By establishing human liver organoids model and high-content imaging method, we demonstrated that MEHP and MBP (2, 10, and 50 mu M) enhanced glucose uptake and lipid accumulation in a dose-dependent manner, promoted glycolysis, and altered key metabolic pathways related to insulin resistance. RNA sequencing and pathway analysis revealed that both MEHP and MBP (100 mu M) selectively upregulated glycolysis-associated genes while suppressing other glucose metabolism pathways, such as the Tricarboxylic acid cycle and Pentose phosphate pathway, leading to increased pyruvate catabolism and lactate accumulation. Furthermore, liver organoids exhibited greater sensitivity to glucose metabolic disruption in response to MEHP than HepG2 cells, highlighting their suitability as a model for studying phthalates-induced hepatotoxicity. Our study provides novel evidence linking phthalate exposure to GDM risk and elucidates the underlying mechanisms through which phthalates disrupt hepatic metabolism.
https://doi.org/10.1016/j.ecoenv.2025.119305

Nuclear Receptor Networks as the Central Hub of Endocrine-Disrupting Chemical Neurotoxicity: A System Toxicology Perspective,
Lu, Y., Ren, L., Yu, J., Zhang, T. and Zhang, J., *Environmental Science & Technology*, 2025/12/31 2025.

Endocrine-disrupting chemicals (EDCs) are ubiquitous environmental contaminants linked to rising neurodevelopmental disorders, yet the neurotoxicity of real-world low-dose mixtures remains poorly understood. This review establishes a conceptual framework positioning the nuclear receptor (NR) superfamily as the central integrative hub, where structurally diverse EDC signals converge. Transcending traditional single-chemical paradigms, we detail how mixtures co-opt the NR network through molecular crosstalk, heterodimer competition, and epigenetic reprogramming. Such disruptions trigger pathogenic cascades, including dysregulated neuroinflammation, impaired synaptic plasticity, and bioenergetic collapse, that compromise brain development. We critically evaluate state-of-the-art experimental and computational models, from brain organoids to microphysiological systems, advocating for an integrated systems toxicology approach. Leveraging time-series multiomics and dynamic network modeling is essential to identify mechanistic thresholds and assess potential transgenerational risks. This NR-centered framework provides a robust foundation for evolving the discipline from descriptive toxicology to predictive, next-generation risk assessment, ultimately safeguarding brain health in an increasingly complex chemical environment.
https://doi.org/10.1021/acs.est.5c14620

An Overview of Emerging Per and Polyfluoroalkyl Substances; Environmental Occurrence, Health Effects, Treatment Approaches and Sustainable Alternatives,

Monisha, M., Gopalakrishnan, M., Kulandaivel, T., Janjaroen, D. and Ganesan, S., *Journal of Vinyl & Additive Technology*, 2025.

Emerging Per and polyfluoroalkyl substances (PFAS) have become a growing concern due to their widespread presence, persistence, and potential health hazards. They are broadly classified into polymeric and non-polymeric PFAS. While regulatory initiatives have limited the use of long-chain PFAS such as perfluorooctanoic acid (C8) (PFOA) and perfluorooctane sulfonic acid (C8) (PFOS), industries like food packaging, textiles, firefighting foam, semiconductors, and electronics are now shifting toward short-chain PFAS and novel fluorine-free alternatives. However, these short-chain PFAS have high mobility, environmental persistence, and potential bioaccumulation, raising concern about their long-term effects on human health, wildlife, and ecosystems. These chemicals have been found in several environmental matrices and also in various food products. Exposure to these PFAS, mainly through polluted drinking water, food items, and consumer products, leads to potential health hazards, including liver, kidney, and nerve damage, endocrine disruptions, immune system dysfunction, developmental issues, and increased risk of cancer. Several destructive and nondestructive treatment techniques, including adsorption, membrane technology, advanced oxidation process, photocatalytic degradation, and microbial degradation, have been explored to remove PFAS from various matrices. In addition, scientists and policymakers globally are promoting stricter regulations and the development of sustainable alternatives. This review provides a comprehensive overview of PFAS occurrence, classification, regulatory limits, health impacts, current removal strategies, and highlights various fluorine-free alternatives. https://doi.org/10.1002/vnl.70054

Field cancerization, accelerated aging, and immunosuppression: the rapid rise of hormone-sensitive and early-onset breast cancer,
Parrish, M., Traugh, N., Seraj, M. and Kuperwasser, C., *Npj Breast Cancer*, Nov 18 2025, Vol. 11, no. 1.

Breast cancer etiology traditionally emphasizes genetic mutations, hormonal dynamics, and tissue aging. However, recent decades have seen a steady rise in breast cancer with a growing proportion of these tumors exhibiting estrogen receptor-positive (ER +) phenotypes along with an alarming rise in early-onset breast cancer occurring in individuals without a family history of the disease. While increased screening and lifestyle changes explain part of this trend, they do not fully account for the rising incidence, particularly among specific racial and geographic subgroups. We hypothesize that this rising trend in hormone-sensitive and early-onset cancers is a manifestation of chronic, cumulative environmental exposures, particularly to endocrine-disrupting chemicals (EDCs), that profoundly alter breast tissue biology. Since EDCs alter estrogen receptor signaling, the epigenetic landscape, and disrupt immune surveillance, we hypothesize that this may underpin the rising incidence of hormone-sensitive early-onset breast cancers through a mechanism that affects field cancerization and hormone-mediated aging. https://doi.org/10.1038/s41523-025-00840-w

Environmental Contaminants and Congenital Heart Defects: Focus on PFAS, PAHs, and Other Emerging Exposures,
Patel, J., Weber, K., Upadhyay, R. and Nembhard, W. N., *Clin Chem*, Dec 30 2025, Vol. 72, no. 1, p. 133-139.

BACKGROUND: Congenital heart defects (CHDs) are the most prevalent birth defects, contributing significantly to infant morbidity and mortality. While genetic factors account for a subset of CHDs, environmental exposures during critical periods of cardiac development are increasingly recognized as potential contributors. CONTENT: This review synthesizes current evidence linking per- and

polyfluoroalkyl substances, polycyclic aromatic hydrocarbons, and other environmental contaminants to CHDs. We discuss epidemiological findings, biological mechanisms, exposure assessment methodologies, and future research directions, emphasizing the need for integrated approaches in understanding and mitigating environmental risks to fetal cardiac development. SUMMARY: This review emphasizes the need for integrated approaches in understanding and mitigating environmental risks to fetal cardiac development.
https://doi.org/10.1093/clinchem/hvaf158

A comparative toxicological and epidemiological evaluation of dioxins and PFAS chemicals, Paustenbach, D., Kissell, K. and Shakya, A., *Critical Reviews in Toxicology*, 2025.

Regulatory frameworks, informed by robust and transparent scientific evidence, can significantly benefit society when thoughtful and measured regulation is promulgated. However, regulations founded on incomplete or misinterpreted science often result in unintended consequences. As was the case with the polychlorinated dibenzodioxin and polychlorinated dibenzofuran (PCDD/PCDF) chemicals, for the past 50 years, there has been a lack of scientific consensus on the adverse health effects of per- and polyfluoroalkyl substances (PFAS) in humans at current blood concentrations (about 4 ppb TEQ) or even concentrations 10-300-fold higher (40-1200 ppb TEQ). Despite their distinctly different chemical structures, the dioxins, particularly 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), and perfluorooctanoic acid (PFOA)/perfluorooctanesulfonic acid (PFOS), share notable similarities: environmental persistence, biological recalcitrance, slightly unpredictable acute toxicity, a lack of genotoxicity, and suggestive data on adverse health effects in humans; across a wide range of doses. Both substances display varying degrees of acute toxicity across species, and both have been associated with the onset of wasting syndrome in certain animals at fairly high doses, but wasting syndrome is not seen in humans. Although there is moderate to high acute toxicity in multiple animal species for both families of chemicals, there is low acute toxicity in humans. In humans, both compounds interact with fatty acid metabolism. The evidence indicates that both are either weakly genotoxic or non-genotoxic. The dioxins can cause cancer in a variety of animal species, but even in humans exposed to high doses, no increased cancer risk is apparent. PFAS chemicals are similar; weakly carcinogenic in animals and, perhaps, lacking carcinogenic potency in humans. However, unlike with dioxins, high human exposure to PFAS has only occurred in the workplace; thus, few data from highly exposed human populations are available to rigorously evaluate the human cancer risk or other potential effects at elevated doses. Similar to the widespread presence of dioxins reported in the 1970s-1980s, PFAS chemicals are now globally ubiquitous, with detectable concentrations in nearly every individual, fish, and wildlife species. As awareness has increased over time, pressure to prevent the release or manufacture of PFOA and PFOS has decreased the blood concentrations in Americans by 10-fold over the past 15 years, paralleling trends observed with the dioxins when global concerns surfaced. The dioxins were regulated in a heavy-handed manner despite scientific uncertainty regarding their human health risks over a range of exposure levels, as well as a lack of consensus on dose-response relationships, thresholds for adverse effects, and human relevance of high-dose animal studies. The regulatory actions that occurred with the dioxins ultimately resulted in substantial economic and societal costs, even in the face of much uncertainty. This paper examines the parallels between the development of scientific understanding of the health hazards and the eventual regulation of dioxins and PFAS chemicals. For both families of chemicals, the precautionary principle was followed by most agencies rather than solid scientific data during the rulemaking process.
https://doi.org/10.1080/10408444.2025.2560827

Prenatal Dietary Exposure to Endocrine Disruptors and Its Lasting Impact on Offspring Health,

Potiris, A., Daponte, N., Moustakli, E., Zikopoulos, A., Kokkosi, E., Arkouli, N., Anagnostaki, I., Vogiatzoglou, A. L., Tzeli, M., Sarella, A., Domali, E. and Stavros, S., *Toxics*, Oct 11 2025, Vol. 13, no. 10.

Environmental stressors during the crucial period of fetal development can have a substantial impact on long-term health outcomes. A major concern is dietary exposure to endocrine-disrupting chemicals (EDCs), which can readily cross the placenta and disrupt fetal hormonal signaling and developmental programming. Examples of these chemicals include bisphenols, phthalates, pesticides, and persistent organic pollutants (POPs). Prenatal exposure to EDC has been associated with long-term effects in children, including immune disruption, metabolic dysregulation, impaired neurodevelopment, and reproductive alterations, as evidenced by human cohort studies and experimental models. Epigenetic reprogramming, direct interference with endocrine signaling, and oxidative stress (OS) are hypothesized pathways for these adverse consequences, which often combine to produce long-lasting physiological changes. This narrative review summarizes current research on maternal dietary exposure to EDCs during pregnancy, highlighting associations with adverse child health outcomes. It also discusses the growing evidence of transgenerational effects, the potential mechanisms linking prenatal exposure to long-term outcomes, and the importance of understanding the roles of timing, dosage, and chemical type. By highlighting the necessity of focused interventions to lower maternal EDC exposure and lessen threats to the health of offspring, the review concludes by discussing implications for future research, preventive measures, and public health policy. https://doi.org/10.3390/toxics13100864

In vivo effects of cadmium on signaling and secretion of pituitary gonadotrophs in male mice are time-dependent,
Santiago-Andres, Y., Alvarez, E. H., Gutierrez, D. O., Bermea, O. M. and Fiordelisio, T., *Journal of Endocrinology*, Oct 1 2025, Vol. 267, no. 1.

Cadmium is a heavy metal found widely in the environment, originating from industrial emissions, mining activities, phosphate fertilizers, and cigarette smoke. It is an endocrine-disrupting chemical that mimics essential metals such as calcium and zinc, interfering with hormone signaling. Due to its long biological half-life, cadmium bioaccumulates in organisms, raising concerns about its long-term effects on endocrine and reproductive health. Cadmium's reproductive toxicity is well documented, with studies highlighting its impact on gonadotropin regulation and testicular function. However, its specific effects on calcium (Ca2+) signaling in gonadotrophs remain poorly understood. This study aims to determine whether cadmium disrupts Ca2+-dependent signaling mechanisms essential for gonadotropin secretion. To address this, we used an adult male mouse model to assess pituitary cadmium accumulation, gonadotroph responsiveness to GnRH, and alterations in Ca2+ mobilization patterns. Our results show that cadmium exposure leads to pituitary bioaccumulation, prolonged endocrine disruption, and gonadotroph hyperplasia. Initially, gonadotroph responsiveness to GnRH declines, but over time, altered Ca2+ oscillation patterns and increased gonadotropin secretion emerge. A transition from normal oscillatory Ca2+ signaling to biphasic responses was observed, along with sustained phospholipase C-beta (PLC beta) activation, suggesting persistent intracellular signaling disruptions. In addition, cadmium exposure resulted in testicular atrophy, increased apoptosis, and reduced sperm count. Testosterone levels declined, while the gonadotroph population increased, highlighting an imbalance in endocrine regulation. These findings suggest that cadmium induces reproductive toxicity through a combination of direct testicular damage and disruption of gonadotroph calcium signaling and hormone secretion, leading to testicular dysfunction that is relevant to public health. https://doi.org/10.1530/joe-25-0161

Impact of Endocrine-Disrupting Chemicals (EDCs) Used in the Food Industry on Endocrine Abnormalities,
Serrano-López, P. D., Ocampo-Juárez, F. B., Magaña-Rodríguez, A. and Téllez-Morales, J. A., *Food Safety and Health*, Oct 2025, Vol. 3, no. 4, p. 547-556.

The objective of this review was to examine the relationship between hormone disruption and other endocrine abnormalities in the context of the constant consumption of genetically modified foods and overexposure to chemicals used directly and indirectly in the agrifood industry. This review collates data pertinent to endocrine health and its correlation with dietary intake and the chemical substances that come into contact with food, including pesticides. We hypothesized that the changes caused by genetically modified organisms (GMOs) may have metabolic effects in the medium and long term, such as the proliferation of adipose tissue. Importantly, the scientific evidence on which we can rely has different slopes due to the types of studies and experiments necessary to verify them, as is the case for metabolic disorders, cancers of the gastrointestinal tract, and GMOs. Finally, it is imperative to acknowledge that the repercussions of disruptive compounds-which encompass, but are not limited to, pesticides and genetically modified organism derivatives-require additional investigation. https://doi.org/10.1002/fsh3.70033

Phthalates and epigenetics: An emerging public health concern,
Singh, A., Khan, N., Choudhury, M., Rai, P. S. and Kabekkodu, S. P., *Current Research in Toxicology*, 2025 2025, Vol. 9.

Phthalates are a group of phthalic acid esters that are commonly used as plasticizers in many consumer products to improve elasticity, transparency, durability, and toughness. Phthalates are also ubiquitously found throughout our environment. In recent years, research has indicated a growing concern over the potential negative health effects that phthalates have on the human body. Considering their presence in a wide range of consumer goods, including food packaging, household goods, medical equipment, and personal hygiene products, humans are continuously exposed to many phthalates in their everyday lives. More strikingly, exposure to phthalates has been shown to induce abnormal epigenetic changes in noncoding RNA expression, DNA methylation, and histone modification. Epigenetic changes are critical in governing gene expression while leaving the DNA sequence intact. Previous studies have established the role of aberrant epigenetic changes in the pathogenesis of many diseases, including cancer and endocrine diseases related to phthalate exposure. The purpose of this review is to provide insight into the mechanisms by which phthalates may affect epigenetic processes and the potential adverse health consequences of these interactions. https://doi.org/10.1016/j.crtox.2025.100267

Effects of Endocrine-Disrupting Chemicals in the Brain: The Example of Neurodevelopment Alterations upon Exposure In Utero to Synthetic Sex Hormones,
Sultan, C., Gaspari, L. and Soyer-Gobillard, M. O., *Journal of Xenobiotics*, Oct 10 2025, Vol. 15, no. 5.

Endocrine disruptors contaminate indoor and outdoor air, water, and food. Besides modifications of the androgen/estrogen balance, endocrine disruptors can alter thyroid function, metabolic balance, immune defenses, and brain development during fetal life, childhood, and adolescence. Among the consequences of fetal exposure to endocrine disruptors, neurobehavioral disorders, particularly psychiatric disorders (for example, schizophrenia and bipolar disorder), attention deficit disorders, and mood disorders, occupy a special place. Therefore, endocrine disruptors are also neuroendocrine disruptors. This review article first summarizes the direct and transgenerational effects of endocrine disruptors. Then, data from a French national cohort of patients whose mothers were treated with synthetic hormones (estrogens and/or progestogens) during their pregnancy(ies)

are used to describe the psychiatric disorders developed by children exposed in utero and the multigenerational and potentially transgenerational impacts. https://doi.org/10.3390/jox15050162

Another pleiotropic effect of SGLT2 inhibitors: Is it a new frontier in thyroid function regulation?, Szklarz, M., Wołos-Kłosowicz, K., Szulc, J., Górny, J., Modzelewski, R. and Matuszewski, W., *Thyroid Res*, Jan 5 2026, Vol. 19, no. 1, p. 2.

In our review, we present possible hypotheses that might explain how sodium glucose cotransporter 2 (SGLT2) inhibitors affect thyroid function. We describe mutual interactions between thyroid hormones and the development of diabetes and obesity. We show the effects of other antihyperglycemic drugs on thyroid hormone changes. We demonstrate how endocrine-disrupting chemicals (EDCs) may act as potential triggers for the development of thyroid disease, obesity and diabetes, and how SGLT2 inhibitors may constitute a potential protective barrier against their negative effects. We describe mechanisms of the immunomodulatory and antioxidant effects of flozins, that may reduce the risk of autoimmune thyroid disease (AITD). We describe beneficial effects of flozins on heart and kidney function, that may also contribute to thyroid protection. Finally, we present a hypothesis of a possible favourable effect of SGLT2 inhibitors on Graves' orbitopathy (GO), myocardial protection in hyperthyroidism, and a reduction in the risk of thyroid cancer. Aim of our work is to summarise current evidence and hypotheses regarding SGLT2 inhibitors and thyroid function. However, it should be borne in mind that there are still limited clinical evidence about impact of flozins on thyroid metabolism.Clinical trial number Not applicable. https://doi.org/10.1186/s13044-025-00282-3

Real-life organochlorine mixture-induced lipid dysregulation and oxidative stress in Leydig TM3 cells: Mechanistic insights into male reprotoxicity,
Virmani, I., Sychrová, E., Rehurková, E., Gadara, D., Spácil, Z., Novák, J. and Sovadinová, I., *Toxicology*, Jan 2026, Vol. 519.

Persistent environmental pollutants such as organochlorines (OCs) remain a global concern due to their widespread distribution, bioaccumulative nature, and endocrine-disrupting potential. While associations with male reproductive toxicity are well documented, the underlying mechanisms, particularly those involving lipid metabolism in testicular cells, are not fully understood. This study investigates the mechanistic basis of male reprotoxicity induced by a real-life OC mixture (OC-MIX), modeled after the contaminant profile of ringed seal blubber and comprising 20 environmentally relevant OCs, including pesticides (e.g., dichlorodiphenyltrichloroethane) and industrial compounds (e.g., polychlorinated biphenyls). We applied a mechanistic in vitro test battery that combines receptor-specific reporter gene assays with functional profiling in immature murine Leydig TM3 cells exposed to OC-MIX concentrations ranging from 0.04 to 50 mu g/mL. OC-MIX exhibited strong antiandrogenic and dioxin-like activities. Functional assays revealed reduced testosterone and progesterone levels, increased oxidative stress, and impaired mitochondrial function. These effects were driven by broad lipid dysregulation, including enhanced fatty acid degradation and acylcarnitine depletion, which was evident even at the lowest tested concentration (2.5 mu g/mL). These lipid alterations were not primarily mediated via androgen receptor antagonism or aryl hydrocarbon receptor agonism. Instead, the lipidomic signature closely resembled that of the lipotoxic drug amiodarone, rather than a non-cytotoxic fatty acid mixture. Our findings underscore the central role of lipid metabolism in testicular function and demonstrate that OC-MIX exerts reproductive toxicity via complex, non-classical endocrine mechanisms. This study highlights the value of integrating lipidomics with mechanistic in vitro models to assess the reproductive toxicity of environmental chemical mixtures. https://doi.org/10.1016/j.tox.2025.154332

In vitro evidence for bisphenol A as a human liver carcinogen: Environmentally relevant doses inhibit cancer-protective ESR1 signaling in a human liver cell line,
Weeks, E., Kennedy, S., Searles, R., Carrothers, S., Davis, B., Carbone, L., Turker, M., Lloyd, R. S. and Weinhouse, C., *bioRxiv*, 2025, p. 2025.12.18.695265.

Several environmentally ubiquitous endocrine disrupting chemicals (EDCs) are suspected carcinogens, but their mechanism(s) of action are unknown. In this study, we test the potential for a model EDC, bisphenol A (BPA), to both initiate (via oxidative mutagenesis) and promote (via endocrine disruption) liver carcinogenesis. This study is motivated by our prior finding that developmental BPA exposure caused hepatocellular carcinoma (HCC) in mice. Here, we provide in vitro evidence supporting a mechanism for BPA as a non-genotoxic carcinogen. Using a highly sensitive, error-corrected sequencing method, we demonstrate that human population-relevant doses of BPA cause mutations that are consistent with oxidative DNA damage; however, overall mutation frequency does not differ substantially from controls. In contrast, we show that BPA inhibits cancer-protective, estrogen-induced transcription of estrogen receptor 1 (ESR1) target genes in the presence of pre-pubertal, but not post-pubertal, levels of estradiol. These results constitute strong initial evidence supporting BPA as a liver cancer promoting agent. This mechanism may be generalizable to a wide range of environmental EDCs that are weak agonists for ESR1. This finding is critically important to prevention of HCC, which is prevalent, lethal, and poorly responsive to therapy.Competing Interest StatementThe authors have declared no competing interest.National Institute of Environmental Health Sciences, R01ES034836Oregon Institute of Occupational Health Sciences, OHSU https://doi.org/10.64898/2025.12.18.695265

Real-life per- and polyfluoroalkyl substances mixture impairs placental function: insights from a trophoblast spheroid model,
Xia, Y., Fu, Q. G., Voss, H., Fest, S., Arnold, S., Bauer, M., Fink, B., Zenclussen, A. C. and Stojanovska, V., *Environmental Research*, Dec 15 2025, Vol. 287.

Per- and polyfluoroalkyl substances (PFAS) are persistent endocrine-disrupting chemicals (EDCs) linked to adverse reproductive outcomes. While the placenta is a known target of PFAS toxicity, most in vitro studies use two-dimensional (2D) cell culture models, often focusing on late-pregnancy tissue or blood PFAS concentrations and examining single compound exposures. In this study, we measure placenta PFAS concentrations in early pregnancy and design a placenta-relevant PFAS mixture to assess its impact on trophoblast function using a three-dimensional (3D) trophoblast spheroid model. PFAS levels in first-trimester placental tissue were quantified using liquid chromatography/triple quadrupole mass spectrometry. Six PFAS: perfluorononanoic acid (PFNA), perfluorooctanesulfonic acid (PFOS), perfluorobutanoic acid (PFBA), perfluorooctanoic acid (PFOA), perfluorohexanesulfonic acid (PFHxS), and perfluorodecanoic acid (PFDA); were selected based on their placenta concentrations and relevance to pregnancy complications to design the placenta real-life PFAS mixture. Next, trophoblast spheroids were propagated from two different cell lines, JEG-3 and HTR-8/SVneo, to assess the effects of PFAS mixture on trophoblast viability, apoptosis, invasion, hormone production, and gene expression. While trophoblast spheroid viability remained largely unaffected, we observed changes in trophoblast function. PFAS exposure significantly increased invasiveness in JEG-3 spheroids at 48 h, but markedly reduced it in HTR8/SVneo spheroids at 96 h across varying concentrations. Additionally, pregnancy-specific hormone e.g. beta-hCG production declined after 48 h of PFAS mixture exposure in JEG-3 spheroids. Gene expression analysis revealed altered apoptosis and proliferation pathways in both trophoblast spheroids. Overall, our study highlights that physiologically relevant 3D trophoblast models can contribute to the broader comprehension of PFAS-associated reproductive health risk assessments.
https://doi.org/10.1016/j.envres.2025.123037

Epigenetic and epitranscriptomic landscape of phthalate toxicity: Implications for human health and disease,
Ye, Z., Mayila, M., Bu, N., Hao, W. and Maimaitiyiming, Y., *Environ Pollut*, Feb 15 2026, Vol. 391, p. 127559.

Phthalates (PAEs) are endocrine-disrupting chemicals widely used in industrial applications, with significant implications for human health. Growing evidence highlights epigenetic and epitranscriptomic mechanisms, specifically DNA methylation, histone modification, RNA modification and non-coding RNAs, as pivotal mediators of PAE toxicity. This review synthesizes current knowledge on how PAEs disrupt these regulatory layers, linking their dysregulation to diseases such as psoriasis, diabetes, atherosclerosis, reproductive disorders, and cancer. We recapitulate PAE-induced alterations in global and gene-specific DNA methylation patterns, chromatin remodeling via histone acetylation and methylation, and dynamic RNA modifications, alongside the aberrant expression of miRNAs and lncRNAs, which collectively drive pathological outcomes. Additionally, we discuss the potential of epigenetic and epitranscriptomic markers as diagnostic tools and therapeutic targets for PAE-associated diseases. By integrating these dual regulatory perspectives, our work bridges a gap in understanding PAE toxicity and underscores the need for interdisciplinary research to mitigate exposure risks. Finally, we outline future directions to unravel long-term epigenetic/epitranscriptomic impacts, offering novel insights into molecular mechanisms and intervention strategies. https://doi.org/10.1016/j.envpol.2025.127559

Comparative assessment of female reproductive toxicity from PFOA and its alternative GenX in mice and human granulosa cells,
Yuan, Y. Y., Wang, B. H., Fan, Y. Y., Le, M. L., Wu, L. H., Deng, S. Y., Huang, J. and Zhang, D. L., *Toxicology and Applied Pharmacology*, Jan 2026, Vol. 506.

Perfluorooctanoic acid (PFOA) is a legacy perfluoroalkyl substance (PFAS) with various detrimental health effects, prompting its replacement by hexafluoropropylene oxide dimer acid (GenX). However, the female reproductive toxicity and underlying mechanism of GenX remain inadequately understood. In this study, we comparatively evaluated the impacts of PFOA and GenX on ovarian function using integrated in vivo mouse and in vitro human granulosa cell models. Our experimental findings indicated that oral exposure to PFOA significantly reduced ovarian weight, impaired follicular development, disrupted estrous cyclicity, decreased estradiol level, and induced ovarian oxidative stress and apoptosis in mice. However, GenX did not display significant toxic effects on the ovaries at the doses tested, except for reducing ovarian GPX4 expression and serum estradiol level. Notably, both PFOA and GenX at high-concentration treatment in vitro dramatically impaired the viability and proliferation, elicited ROS overproduction and mitochondrial injury, and suppressed NRF2 and HO-1 expression in cultured KGN cells. Nevertheless, at equivalent exposure doses, GenX elicited markedly decreased adverse influences on KGN cells compared to PFOA. Molecular docking simulation indicated a stronger interaction of PFOA with NRF2 than GenX. In addition, treatment with PFOA also diminished estradiol secretion and induced apoptosis in KGN cells. In summary, PFOA exposure resulted in female reproductive impairment by inducing oxidative stress and apoptosis in mouse ovaries and human granulosa cells. Although GenX exhibited comparatively low ovarian detriment relative to PFOA, its potential risk of reproductive toxicity remains a nonnegligible concern. https://doi.org/10.1016/j.taap.2025.117639

Unraveling the Obesogenic Mechanism of Bisphenol A Through Network Toxicology and Molecular Docking: Identification of Key Molecular Targets,

Zhang, R. Q., Zhao, M. M., Wen, H. R., Lin, Z. and Zhou, X. B., *International Journal of Molecular Sciences*, Oct 31 2025, Vol. 26, no. 21.

This study integrates network toxicology with molecular docking technology to systematically elucidate the key molecular mechanisms and signaling pathways by which bisphenol A (BPA) induces obesity. By cross-referencing multiple databases-including the Comparative Toxicogenomics Database (CTD), SwissTarget prediction platform, and PharmMapper-potential BPA target genes were identified, yielding a total of 1326 candidate targets. Obesity-related genes were collected from GeneCards and OMIM databases, yielding 4570 disease-associated targets. Among these, 653 overlapping genes were identified as potential mediators linking BPA exposure to obesity. Protein interaction networks were constructed using STRING and Cytoscape, and the MCC algorithm identified five core hub genes: STAT3, MYC, TP53, IL6, and mTOR. Validation using random datasets demonstrated significant upregulation of these genes in the obesity group ($p < 0.05$), highlighting their potential central role in BPA-induced obesity effects. Functional enrichment analysis via GO and KEGG pathways indicated that BPA may promote obesity by interfering with endocrine signaling, activating lipid metabolism, and stimulating atherosclerosis pathways. Molecular docking analysis using CB-Dock2 confirmed strong binding affinity between BPA and core targets, providing structural evidence for their potential interactions. This study elucidates the potential biological mechanism by which BPA exacerbates obesity through endocrine disruption and metabolic reprogramming, employing a multidimensional approach encompassing cross-target analysis, pathway enrichment, and molecular interactions. It provides an innovative systems toxicology framework and empirical basis for assessing metabolic health risks induced by environmental pollutants. https://doi.org/10.3390/ijms262110647

Méthodes

Report on the State of the Science to Address Endocrine Disrupters Under the Globally Harmonised System of Classification and Labelling.
OECD Series on Testing and Assessment, No. 427, *OCDE* (2025),

A variety of chemicals may interfere with the endocrine systems of humans and wildlife. To protect humans and the environment from potential adverse effects, there is interest in identifying such chemicals and classifying the hazard. To evaluate available methods to identify endocrine disrupters under the United Nations Globally Harmonised System for Classification and Labelling of Chemicals (GHS), the OECD convened an expert group to provide input. The expert group reviewed the state of the science for the relatively well studied estrogen, androgen, thyroid, and steroidogenesis (EATS) pathways, as well as other endocrine pathways (i.e. "non-EATS"). Methods were reviewed for their ability to identify chemical interactions with endocrine pathway targets (i.e. mechanism) and associated downstream adverse effects to humans and environmental species. This report summarises the review of the state of the science, methods identified for EATS and non-EATS endocrine disrupters, and the diversity of expert views provided to the GHS.
https://doi.org/10.1787/9aa7cd81-en

The ENDOMIX project: an interdisciplinary approach to understanding how real-life chemical mixtures target the immune system to trigger disease,
Zenclussen, A. C., Belmar Erilkin, V., Böhmert, L., Borilova Linhartova, P., Braeuning, A., Braun, G., Chevrier, C., Duijts, L., Escher, B. I., Felix, J., Gómez-Olarte, S., Guxens, M., Herberth, G., Hilscherova, K., Klanova, J., Kohl, Y., Krischak, K., Lagadic-Gossmann, D., Langouët, S., Llop, S., Lopez-Espinosa,

M. J., Maitre, L., Martin-Chouly, C., Meyer, N., Ouidir, M., Pham, T. a. M., Philippat, C., Pieters, R., Pinel-Marie, M. L., Podechard, N., Polte, T., Price, E., Robinson, O., Schubert, K., Schumacher, A., Stojanovska, V., Tal, T., Vineis, P., Van Vorstenbosch, R., Vermeulen, R. and Warembourg, C., *Open Res Eur*, 2024, Vol. 4, p. 271.

The true impact of endocrine disrupting chemicals (EDCs) on human health is far from being understood. Humans are exposed to mixtures of chemicals throughout their lives, yet regulations and most studies focus on individual chemicals. ENDOMIX takes a novel approach to identifying associations and causality between EDCs and adverse health outcomes by focusing on exposure to mixtures of EDCs over the life course, including windows of susceptibility, using human biomonitoring data from several European cohorts. We will model and measure how real-life EDC mixtures act together and target the immune system to initiate, trigger or maintain disease. Health effects will be investigated using pioneering methodologies ranging from high-throughput in vitro bioassays, sophisticated organoid and co-culture systems, to in vivo models. In combination, they will provide valuable information on mechanistic pathways and transgenerational effects of EDC exposure. We aim to identify biomarkers and patterns of chemical exposures that are easy to measure, available for large cohorts and indicative for adverse health outcomes. We will use in vitro, in silico and in vivo data to strengthen causal inference using a weight-of-evidence approach. Moreover, using novel text mining methods, we will create knowledge graphs to capture and summarize the complexity of biomechanistic information, which aids rapid risk assessments and the creation of network models. The knowledge generated by ENDOMIX will provide an evidence base for policy-making and also reach people of all ages to raise awareness of the risks of EDC exposure and encourage health-promoting behaviors. https://doi.org/10.12688/openreseurope.19088.2

A pragmatic upstream network for disrupted steroidogenesis through reduced enzyme activity and steroid hormone production for Adverse Outcome Pathway building,
Bouftas, N., Rosenmai, A. K., Panagiotou, E. M., Zilliacus, J., Damdimopoulou, P., Beronius, A., Van Duursen, M. and Svingen, T., *Reproductive Toxicology*, Jan 2026, Vol. 139.

The Adverse Outcome Pathway (AOP) framework offers a structured approach to organize mechanistic knowledge of toxicological pathways. By describing biological events linking molecular initiating events (MIEs) to an adverse outcome (AO) at the organismal level, it aims to aid regulatory decision-making through predictive toxicology approaches. To serve this purpose, however, it is recognized that AOP networks are required to adequately capture complex biology. Another central feature of the AOP concept is that upstream molecular networks will be shared between numerous downstream AOs. This report focuses on steroidogenesis, a common target of endocrine disrupting chemicals, and the development of an upstream network for reduced steroidogenesis focusing on hormones and enzymes that are particularly relevant to mammalian reproduction. The AOPWiki was mapped for existing content related to steroidogenesis and the resulting network expanded by incorporating additional key events (KEs) and KE Relationships (KERs) not yet inventoried. All existing KEs and KERs were evaluated for completeness. Using a pragmatic approach, we developed the identified KEs and KERs by integrating evidence from recent review articles. The focus was particularly on the impact of disrupted cholesterol transport, altered enzyme activities and hormone levels. The resulting upstream AOP network serves as a foundation for developing complete AOPs linking disrupted steroidogenesis with downstream AOs. This upstream network will also contribute to identifying relevant test assays for development and understanding the predictive capabilities of existing in vitro assays, such as the OECD-validated H295R steroidogenesis assay.
https://doi.org/10.1016/j.reprotox.2025.109105

Screening and prioritization of endocrine-disrupting chemicals in plastic toys for children based on non-target analysis and machine learning predictive model,
Cai, W. W., Li, S. Y., Zhang, Y. C., Zhao, B. Y., Wang, K. K., Li, X., Li, X., Li, J., Ying, G. G. and Cao, Z. G., *Environment International*, Nov 2025, Vol. 205.

The health risks associated with the exposure of infants to harmful chemicals, particularly endocrine disruptors, in plastic toys have garnered widespread attention; however, the corresponding knowledge remains limited. In this study, we employed a non-target analysis approach alongside Toxicological Priority Index (ToxPi) model based on toxicity data predicted by machine learning predictive model to systematically screen and prioritize endocrine-disrupting chemicals (EDCs) in plastic toys for very young children (n = 45). A total of 165 compounds were identified and classified into five categories: additives (30.3 %), processing aids (13.3 %), monomers and intermediates of synthetic plastics (11.5 %), non-intentionally added substances (10.9 %), and uncategorizable chemicals (33.9 %). Among these, antioxidants, plasticizers, flame retardants, and surfactants were widely detected. Emerging non-phthalate plasticizers and non-intentionally added drugs were reported for the first time in this study. In addition to the known EDCs (e.g., phthalates), the endocrine disruption prediction results indicated that antioxidants (n = 8) and antibacterial agents (n = 2) exhibited high ToxPi scores among the identified chemicals. Further, exposure risk index was calculated by incorporating both ToxPi scores and the peak intensities of the compounds identified above. Toys made from polyethylene terephthalate, silicone, acrylonitrile-butadiene-styrene, and polystyrene had higher risk index compared with those made from polypropylene. The antibacterial agent ethyl sorbate, antioxidant Irganox 1010, therapeutics/prescription drugs dienogest, and antibacterial agent chalcone were identified as top priority EDCs in each material. This study highlights the urgent need to assess the exposure risks for infants through plastic toys and to implement control measures for emerging EDCs in plastic toys for very young children. https://doi.org/10.1016/j.envint.2025.109878

Negative Paper Spray Ionization Mass Spectrometry for the Determination of Endocrine-Disrupting Chemicals with Application to Paraben Analysis in Cosmetics,
Cho, S., Amatya, S. S., Bahng, H., Lee, E., Ko, Y. and Cha, S., *Molecules*, Nov 10 2025, Vol. 30, no. 22.

Paper spray ionization mass spectrometry (PSI-MS) enables rapid analysis with minimal sample preparation, yet negative-ion mode performance has been limited by poor sensitivity and unstable signals, similar to conventional electrospray ionization. In this study, we optimized negative PSI tandem MS (MS/MS) for twelve endocrine-disrupting chemicals (EDCs) and related biomarkers-including bisphenols, phthalates, parabens, and substituted phenols-used as model analytes. A systematic solvent and additive screen identified 1 mM ammonium fluoride in methanol and 0.1% ammonium hydroxide in 9:1 MeOH/carbon tetrachloride as optimal conditions, providing enhanced deprotonated-ion intensities and improved stability. Calibration curves generated under these conditions showed excellent linearity, with limits of quantitation (LOQs) in the low-ppb range. Application to cosmetic formulations demonstrated reliable paraben quantitation. In fortified hand cream, LOQs below 1 mg/kg were achieved, with recoveries of 93-110% and intra- and inter-day precision below 10% RSD. Notably, PSI-MS/MS performance was comparable to LC-MS/MS, without a separation step. These results demonstrate the feasibility of optimized negative PSI-MS as a sensitive and robust tool for paraben determination in cosmetics and highlight its potential as a versatile platform for broader EDC quantification. https://doi.org/10.3390/molecules30224356

Unveiling the presence of micro and nanoplastics in human biological matrices: A systematic review covering the latest five years from 2020 to 2025,

Christodoulou, M. C., Stylianou, M., Voukkali, I., Naddeo, V., Barcello, D., Kepertis, C. and Zorpas, A. A., *Sci Total Environ*, Dec 29 2025, Vol. 1013, p. 181304.

Plastic contamination has emerged as one of the most pressing environmental challenges of the 21st century, with global plastic production surpassing 413 million metric tons in 2024. This dramatic increase has led to a parallel rise in the generation of micro- and nanoplastics (MNPs), tiny plastic particles that now permeate not only natural ecosystems but also human environments. Human exposure to MNPs occurs through contaminated food, water, inhalation of airborne particles, dermal contact, and medical devices, although the exact exposure levels and health impacts remain uncertain. Once internalized, these particles have been shown to provoke inflammation, oxidative stress, and immune system disruption. To better understand the scope of this issue, a systematic review was conducted in accordance with PRISMA guidelines. Data were extracted on polymer types, particle sizes, detection methodologies, and documented biological impacts. MNPs were consistently identified across a wide range of human biological matrices, with the blood (30.2 %), stool (12.3 %), and skin (9.9 %) being among the most frequently studied. The most detected polymers included polyethylene (PE), polypropylene (PP), and polystyrene (PS). Recent advancements in detection technologies, particularly micro-Raman spectroscopy (µRaman), micro-Fourier Transform Infrared spectroscopy (µFTIR), and pyrolysis gas chromatography-mass spectrometry (Py-GC/MS), have significantly enhanced analytical sensitivity, allowing for the reliable identification of particles as small as 1 µm. Without limitation the results from this systematic review are useful and applicable to guiding public health policies, shaping environmental regulations, and informing future toxicological research.
https://doi.org/10.1016/j.scitotenv.2025.181304

A new alternative method using cyp3a65 expression in transgenic zebrafish embryos to assess metabolic endocrine-disrupting chemicals in the intestine,
Erradhouani, C., Geffroy, F., Piccini, B., Hinfray, N., Chadili, E., Balaguer, P., Sohm, F., Aït-Aïssa, S., Coumoul, X. and Brion, F., *Environment International*, Nov 2025, Vol. 205.

Metabolic endocrine-disrupting chemicals (MDCs) contribute to the development and increasing incidence of metabolic disorders, highlighting the need for relevant assays to identify them. Several alternative models to mammals, notably the zebrafish, have been developed, but none of these assays account for the modes of action and effects of MDCs on the intestine. This study aimed to 1) establish and characterize a transgenic embryo model expressing GFP under the control of the zebrafish cyp3a65 gene, ortholog of the human cyp3a4; 2) set up an original zebrafish embryo-based bioassay to study the Effects of Metabolic Endocrine disRuptors in Gut of zebrafish Embryos (EMERGE). Spatiotemporal expression of cyp3a65-GFP and temporal expression of endogenous cyp3a65 was characterized using fluorescence imaging of GFP, immunohistochemistry and RT-qPCR, under both normal and exposed conditions to clotrimazole and TCDD (respectively zfPXR and zfAhR2 agonists). Then, twenty-two chemicals were screened for their potential activity using the EMERGE assay. We report an early and dynamic expression of cyp3a65 in the developing intestine which is disrupted in a time and concentration dependent manner by zfPXR and zfAhR2 agonists. Moreover, we report that various environmental chemicals can significantly up-or down regulate cyp3a65 expression, most of them being newly identified as targeting the intestine and disrupt this critical metabolic enzyme. In conclusion, EMERGE represents a new easy to use assay to screen metabolic disrupting activity of chemicals in a non-mammalian model. The data collected suggest it could provide valuable insights into the effects of substances on cyp3a4 in humans and may emerge as a valuable assay for assessing human-relevant effects. https://doi.org/10.1016/j.envint.2025.109872

A direct LC–MS/MS method for simultaneous quantitation of bisphenol S, propylparaben, monobutyl phthalate, and their metabolites in human urine,
Gerona, R., Sovereign, A. and Hunt, P., *ChemRxiv*, 07 janvier 2026 2026.

Accurate biomonitoring of non-persistent endocrine-disrupting chemicals (EDCs) requires robust quantitative methods for reliable human exposure and risk assessment. Building on previous work showing that direct measurement of bisphenol A and its conjugated metabolites in human urine reveals substantial underestimation in commonly used indirect, hydrolysis-based approaches, this study addresses the broader need for direct assays of other short-lived EDCs. Here, a direct liquid chromatography–tandem mass spectrometry method is developed and validated for the simultaneous quantification of bisphenol S (BPS), propylparaben (PP), monobutyl phthalate (MBP), and their major glucuronide and sulfate conjugates in human urine, and its performance is systematically compared with that of indirect enzymatic hydrolysis–based methods. Chromatographic separation was achieved on a C18 column with gradient elution, and detection employed negative electrospray ionization in multiple reaction monitoring mode. The method exhibited excellent linearity ($r^2 > 0.995$), low limits of detection (≤0.1 ng/mL for all analytes except BPS glucuronide), and high precision (CV ≤ 7%) and accuracy (relative error ≤ 10%), fulfilling the U.S. FDA bioanalytical validation criteria. Solid-phase extraction provided quantitative and reproducible recoveries with minimal matrix effects and no detectable carryover. Comparison with indirect enzymatic hydrolysis demonstrated close agreement for BPS and PP but revealed concentration-dependent underestimation of MBP (down to ~65% recovery at higher concentrations) using the indirect method. Application of the validated method to urine samples from 30 second-trimester pregnant women showed that glucuronidated forms accounted for >90% of total analyte concentrations and that total BPS, PP and MBP levels exceeded contemporary National Health and Nutrition Examination Survey (NHANES) estimates. Our findings demonstrate that direct approaches can provide more accurate EDC biomonitoring data, highlighting the need to reevaluate exposure estimates derived from indirect methods in population studies.
https://chemrxiv.org/engage/chemrxiv/article-details/6956e867098cdc781f3c5e47

MXene and covalent organic framework heterostructure for efficient extraction of endocrine disrupting chemicals in food,
Huang, J.-Q., Han, Y., Ha, W., Zhang, Y.-S. and Shi, Y.-P., *Journal of Chromatography A*, 2026/01/11/ 2026, Vol. 1766, p. 466629.

Establishing highly sensitive analytical methods to monitor endocrine disrupting chemicals (EDCs) is essential to ensure food safety and human health. Herein, we report a nanoarchitectonics approach to fabricate a MXene and COF heterostructure (Ti3C2TX/TAPT-TFTA) via in situ growth of a β-ketoenamine-linked COF on the Ti3C2TX MXene. The Ti3C2TX/TAPT-TFTA exhibits remarkable extraction capacity for EDCs. The extraction mechanism was systematically investigated through experiments and density functional theory (DFT) calculations. Thus, an analytical method of EDCs employing Ti3C2TX/TAPT-TFTA as dispersive solid-phase adsorbent was established, coupled with HPLC-PDA. The method achieved detection limits of 0.003–0.006 μg·mL-1 with a linear range of 0.020–1.00 μg·mL-1, while recoveries of 79.4–109.9 % and the relative standard deviations of 0.1–6.1 %. These results validate the proposed method as a reliable and effective approach for the sensitive determination of EDCs in complex food matrices, such as beef, chicken, and pork samples.
https://doi.org/https://doi.org/10.1016/j.chroma.2025.466629

Dimerization-Driven Quantitative Modeling of Endocrine Disruption via Sex Hormone Receptors: Divergent Predictions for Estrogen Receptor α and Androgen Receptor,

Jin, J. S., Huang, F. Y., Chen, Q. C., Yu, H. X., Tan, H. Y. and Shi, W., *Environmental Science & Technology Letters*, 2025.

Interactions between endocrine-disrupting chemicals (EDCs) and nuclear receptors (NRs) are extensively used in virtual screening. However, most models overlook receptor dimerization. Here, we systematically investigate the dimerization dependencies of estrogen receptor alpha (ER alpha) and androgen receptor (AR) via big data mining, reporter gene assays, and molecular simulations and further construct a dimerization-driven quantitative framework for endocrine disruption prediction. Database analysis revealed that ER alpha predominantly functions as homodimers whereas AR primarily exists as monomers. Experiments and simulations further demonstrated that ER alpha forms stable dimeric complexes (agonist-ER alpha dimer-coactivator and antagonist-ER alpha dimer-none systems) while AR maintains stability as a monomer (ligand-AR monomer-coregulator system). Based on these mechanistic insights, receptor-specific quantitative models were developed and applied to predict the endocrine-disrupting potential of representative EDCs, including bisphenols and hydroxylated polybrominated diphenyl ethers. These dimerization-informed models showed robust performance for ER alpha dimers (R 2 = 0.605-0.726), whereas AR's monomeric configuration yielded superior predictive accuracy (R 2 = 0.788-0.909). These predictive patterns match their mechanisms. Estrogenic disruption critically depends on dimerization and coactivator recruitment, while antiestrogenic activity appears to be primarily dependent on dimerization and largely independent of corepressor involvement. In contrast, AR disruption is primarily driven by ligand binding and coregulator interactions with minimal dimerization involvement. This framework provides an effective, mechanism-grounded alternative to EDC screening. https://doi.org/10.1021/acs.estlett.5c01043

Comparative analysis of OECD guideline data and Tox21 assays to improve reproductive and developmental toxicity prediction,
Kwon, H. J., Lee, H., Lee, S., Ko, W., Yun, S. J., Uesawa, Y. and Jung, J., *Sci Rep*, Dec 23 2025.

Reproductive and developmental toxicities pose major challenges in chemical safety evaluation because adverse effects can span generations. Conventional in vivo OECD Test Guideline (TG) assays provide robust hazard characterization but require large animal cohorts and extended study periods. In this study, datasets from OECD TG-compliant studies were compiled to identify the mechanistic drivers of toxicity. To complement these data, we integrated high-throughput in vitro results from the U.S. Tox21 program, which evaluates > 10,000 chemicals in human cell-based assays targeting nuclear receptor modulation, oxidative stress, and DNA damage. By aligning OECD TG outcomes with Tox21 profiles, we assessed the associations between in vivo reproductive/developmental toxicity and in vitro mechanistic endpoints using the Toxicity Predictor program. Our analysis suggested that OECD TG 414-, TG 421-, and TG 422-positive chemicals were negatively associated with thyroid-stimulating hormone receptor (TSHR) antagonists, farnesoid X receptor (FXR) antagonists, peroxisome proliferator-activated receptor delta (PPAR δ) antagonists, transforming growth factor beta (TGFβ) agonists, and endoplasmic reticulum stress response (ERsr) agonists in the Tox21 assays. Conversely, OECD TG 416- and TG 443-positive chemicals showed a positive association with histone deacetylase (HDAC) antagonists. Overall, the regulation of miRNA transcription, nuclear receptor activity, and transcription pathways showed significant associations that may indicate key mechanistic links between in vitro and in vivo datasets. These associations may provide supportive insights for considering how alternative data sources could complement existing regulatory toxicology frameworks. https://doi.org/10.1038/s41598-025-33419-3

Biomonitoring of Parabens in South Brazilian Urine Samples: A Validated SPE-LC-MS/MS Method,

Loredo, C. D., Peteffi, G. P., De Souza, C. F., Hahn, R. Z., Grando, A. P., Grassi, G. S., Antunes, M. V. and Linden, R., *Journal of the Brazilian Chemical Society*, 2025 2025, Vol. 36, no. 11.

This study describes a method for the simultaneous parabens (PBs) quantification in 100 urine volunteers residing in Southern Brazil, using a three-step solid-phase extraction (SPE) with hydrophilic-lipophilic balance (HLB (R)) sorbent, with subsequent analysis by liquid chromatographytandem mass spectrometry (LC/MS-MS). This validated approach simplifies the standard five-step SPE process by eliminating the conditioning and equilibration steps. Target analytes included methylparaben (MeP), ethylparaben (EtP), propylparaben (PrP) and butylparaben (BuP). Urine samples (1 mL) were hydrolyzed with beta-glucuronidase acid solution, mixed with deuterated internal standards, and subjected to SPE. Analysis was performed using an UPLC BEH C18 column (2.1 x 100 mm, 1.7 mu m), with a 6.5-min chromatographic run. Intra-assay precision was 2.8-11.6%, inter-assay precision was 0.7-7.1%, and accuracy was 94.8-111.8%. Extraction yields varied from 92.31-109.4%, with matrix effects ranging from -13.7 to -2.8. PBs were measured in all urine samples. A concerning proportion of 3% of the individuals exceeded the recommended acceptable daily intake (ADI) for PrP, indicating a potential health risk (hazard quotient >= 1.0). These findings provide valuable insights into human exposure to PBs in Southern Brazil, highlighting the need for further research to assess potential health risks. https://doi.org/10.21577/0103-5053.20250150

Endocrine Disruptors at the Feto-Maternal Interface: Insight from PBDE Studies and the Utility of Novel Approach Methods,
Menon, R. and Richardson, L. S., *Endocrinology*, Dec 20 2025.

Endocrine mediators are essential for pregnancy maintenance, and their functional withdrawal is associated with normal term and preterm birth (PTB). Therefore, the disruption to endocrine functions or agents that can disrupt endocrine functions are naturally suspected as contributors to PTB. One of the well-studied endocrine-disrupting compounds is Polybrominated diphenyl ether(s) (PBDE). PBDE is a flame-retardant compound that is contained in several products and is a ubiquitous environmental contaminant. PBDE exists in several different congeners, many harmless compounds, but a few PBDE congeners are linked as endocrine disruptors contributing to adverse pregnancy outcomes like PTB. However, data ambiguity suggests that current platforms are insufficient to conclude PBDE's mechanisms of action as an endocrine disruptor at the feto-maternal interface (placenta/fetal membranes). The development of microfluidic-based new approach methods (NAMs) is being introduced to study PBDE and other environmental pollutants. Organs-on-a-chip (OOC) are an emerging class of NAMs that can replicate human organ-level functions in vitro. OOCs are microfluidic systems comprising multiple cell types from an organ that mimics the environment of a physiological organ. These devices are interconnected through microchannels to maintain intercellular interactions. OOC-based testing and development have accelerated globally as regulatory agencies now emphasize the need for reliable, humanized alternatives to traditional animal models. Multiple reproduction-associated OOCs are being developed, and their utility has been tested in assessing mechanisms of action and toxicological parameters of environmental pollutants. This review provides an overview of feto-maternal interface OOCs and uses PBDE as an example to demonstrate how OOCs can study endocrine-disrupting compounds. https://doi.org/10.1210/endocr/bqaf186

QSAR Models for Predicting Oral Bioavailability and Volume of Distribution and Their Application in Mapping the TK Space of Endocrine Disruptors,
Ollitrault, G., Marzo, M., Roncaglioni, A., Benfenati, E., Taboureau, O. and Mombelli, E., *Journal of Xenobiotics*, Oct 15 2025, Vol. 15, no. 5.

Toxicokinetic (TK) properties are essential in the framework of chemical risk assessment and drug discovery. Specifically, a TK profile provides information about the fate of chemicals in the human body. In this context, Quantitative Structure-Activity Relationship (QSAR) models are convenient computational tools for predicting TK properties. Here, we developed QSAR models to predict two TK properties: oral bioavailability and volume of distribution at steady state (VDss). We collected and curated two large sets of 1712 and 1591 chemicals for oral bioavailability and VDss, respectively, and compared regression and classification (binary and multiclass) models with the application of several machine learning algorithms. The best predictive performance of the models for regression (R) prediction was characterized by a Q2F3 of 0.34 with the R-CatBoost model for oral bioavailability and a geometric mean fold error (GMFE) of 2.35 with the R-RF model for VDss. The models were then applied to a list of potential endocrine-disrupting chemicals (EDCs), highlighting chemicals with a high probability of posing a risk to human health due to their TK profiles. Based on the results obtained, insights into the structural determinants of TK properties for EDCs are further discussed. https://doi.org/10.3390/jox15050166

Integrated in silico and in vitro assessment of estrogen and androgen receptor activity of 10 selected PFAS within an Integrated Approach to Testing and Assessment (IATA),
Ortiz, D. M. D., Lee, H., Hoang, N. M. H., Lee, H. J., Choi, J. and Park, K., *Toxicology and Applied Pharmacology*, Jan 2026, Vol. 506.

The potential of per- and polyfluoroalkyl substances (PFAS) to disrupt endocrine systems continues to be a regulatory concern. However, effectively prioritizing these structurally diverse chemicals remains challenging due to inconsistencies in predictive and experimental data. In this study, we employed a multi-tiered evaluation strategy that combines in silico modeling, in vitro assays, and curated mechanistic data within the OECD's Integrated Approach to Testing and Assessment (IATA) framework. Molecular docking using AutoDock Vina, CBDock2, and Endocrine Disruptome consistently revealed strong binding affinities of long-chain PFAS, particularly PFDA, PFOA, and 10:2 FTOH, to estrogen and androgen receptors. These predictions were corroborated by ER and AR transactivation assays (OECD TG 455/458), which demonstrated ER agonist and AR antagonist activity for the same compounds. In contrast, short-chain and sulfonated PFAS (PFHxA, PFBS, PFOS) exhibited limited to no activity across platforms. To enhance the biological relevance of the prioritization, we compiled supporting mechanistic evidence by applying the IATA framework to organize data along the adverse outcome pathway from molecular initiating events, through key events, to predicted adverse outcomes. Literature-reported alterations in steroidogenic enzymes and hormone levels were included to enrich mechanistic depth. All lines of evidences were systematically integrated into a weight-of-evidence matrix, enabling a transparent and biologically plausible ranking of PFAS based on receptor interaction, functional activity, and endocrine-disruptive potential. This combined approach identified PFDA and PFOA as high-priority endocrine disruptors and offers a scalable, non-in vivo strategy for the screening and risk-based prioritization of environmentally persistent chemicals. https://doi.org/10.1016/j.taap.2025.117628

Superior Oxidase-Mimetic Activity of Co-MOF Nanozyme for Smartphone-Based Visually Colorimetric Assay of Mancozeb,
Pang, S., Chen, L., Liu, Y., Lu, X., Liu, H., Shu, Y., Bai, H., Wang, J. and Shi, D., *Molecules*, Dec 12 2025, Vol. 30, no. 24.

Mancozeb (MCZ), a widely used fungicide in agricultural production, has been reported as an environmental endocrine disruptor, posing serious risks to ecosystems and human health. In this work, multivalent Co-MOF nanozymes (MVCM) with excellent oxidase-like activity were synthesized,

which can promote the oxidation of 2,2'-azino-bis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) into a blue oxidative product (ABTS(•+)), with an obvious absorption peak at 415 nm. With the addition of MCZ, the ABTS(•+) was reduced to colorless ABTS through the REDOX reactions between MCZ and ABTS(•+). Based on the unique reducing behavior of MCZ, a nanozyme-based colorimetric detection platform was proposed for the detection of MCZ, with a linear range of 3-27 µM and a detection limit (LOD) of 0.15 µM. Furthermore, the sensor was integrated with smartphones and test strips, establishing a portable smartphone-based platform for the real-time, on-site, and visual quantitative detection of MCZ. The detection concentration range was 15-90 µM, with LOD as low as 15 µM. The assay exhibited high adaptability in practical applications. In summary, this work provided a simple, accurate, and low-cost approach for visual determination of MCZ without complicated instruments and procedures. https://doi.org/10.3390/molecules30244758

Using simulations to explore the conditions under which "true" dose-response relationships are detectable for environmental exposures: polychlorinated biphenyls and birthweight: a case study,
Siegel, E. L., Lamb, M., Goldsmith, J., Rundle, A., Neophytou, A., Berkovitch, M., Cohn, B. and Factor-Litvak, P., *American Journal of Epidemiology*, 2025.

In environmental epidemiology, we use systematic reviews to evaluate the evidence of exposure-outcome relationships with an eye towards regulation. Conflicting results across studies thwart consensus on toxicity. In humans, only observational data is available from studies of environmental exposures, complicating the construction of dose-response relationships across the full range of exposure levels. Individual studies often lack the complete range of exposure levels because environmental exposure levels are tied to study settings. Pooling data across populations seems a natural solution, but strong population-dependent confounding may bias dose-response curves. Using the oft-debated association of polychlorinated bi-phenyls and birthweight as a case study, we describe simulations used to investigate the relative impacts of exposure range-dependent power limitations and confounding on our ability to correctly identify an assumed linear dose-response curve across a representative exposure range. While varying levels of confounding minimally biased estimates in our pooled and meta-analyses, we report very low confidence to ascertain a set underlying dose-response relationship in low-exposure cohorts with a narrow exposure distribution, but high ability in high-exposure cohorts with wide exposure distributions. Our simulations suggest that pooling and meta-analysis should be prioritized despite possible differences in confounding structures, particularly when exposure distributions in individual cohorts are limited. This article is part of a Special Collection on Environmental Epidemiology. https://doi.org/10.1093/aje/kwaf020

Constructing cationic hydroxyl-functionalized hypercrosslinked polymer for effectively enriching and detecting phenolic endocrine disruptors in green shrimp, Basa fish and milk,
Xiao, N., Dong, Y. L., Zhao, Y., Wang, Q. Q. and Wu, Q. H., *Food Chemistry*, Dec 30 2025, Vol. 497.

Developing sensitive and accurate methods for detecting endocrine-disrupting chemicals (EDCs) is highly significant. Herein, a hydroxy-functionalized cationic hypercrosslinked polymer (OH-iHCP) was synthesized for the first time. The OH-iHCP has good adsorption properties for phenolic EDCs. The adsorption mechanism of EDCs on OH-iHCP mainly includes pi-pi stacking, hydrogen bond and electrostatic interaction. A highly viable analytical method for determination of trace EDCs in green shrimp, Basa fish and milk was established by employing OH-iHCP as solid phase extraction adsorbent combined with liquid chromatography-mass spectrometry. The detection limit of the method was 1.45-4.50 ng g- 1, 3.00-7.00 ng g- 1 and 0.04-0.15 ng mL- 1 for green shrimp, Basa fish and milk, respectively. The recoveries of the method were 80.7 %-118 %, with the relative standard deviation less than 8.0 %. This study demonstrates that the developed OH-iHCP could be served as a*

valuable adsorbent for adsorption and separation of phenolic organic pollutants. https://doi.org/10.1016/j.foodchem.2025.147075

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*, Nov 12 2025, Vol. 23, no. 1.

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. https://doi.org/10.1186/s12967-025-07223-6

Agenda, actualité, politique et évaluation de l'exposition

Comment se protéger des perturbateurs endocriniens ? 600 étudiants vont mesurer leur exposition aux polluants pendant un an,
France 3 région (octobre 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 protéger. Avec des petits gestes qui, cumulés, peuvent tout changer. 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

De l'hexane dans nos aliments : le scandale sanitaire que les consommateurs ignorent,
Le Nouvel Obs (15 décembre 2025),
Dans cette tribune, ONG et associations de consommateurs appellent les pouvoirs publics à interdire l'usage, dans l'industrie agroalimentaire, de l'hexane, un solvant neurotoxique, suspecté d'être reprotoxique et perturbateur endocrinien et à promouvoir les alternatives, qui existent.
https://www.nouvelobs.com/opinions/20251215.OBS110677/de-l-hexane-dans-nos-aliments-le-scandale-sanitaire-que-les-consommateurs-ignorent.html

Draft Community Rolling Action Plan (CoRAP) update for years 2026-2028,
(décembre 2025),
The draft is for an annual update of the CoRAP and covers the three subsequent years 2026-2028. It contains substances suspected of posing a risk to human health or the environment. Substance evaluation is the process under REACH Regulation (EC) No 1907/2006 (Articles 44 to 48) that allows generation of information for clarification of such potential risks1. The draft CoRAP contains 28 substances, including 8 new substances compared to the current CoRAP 2025-2027; 17 substances are being planned for evaluation in 2026, including one group, and 10 substances are divided for evaluation in 2027 and 2028. One substance is proposed to be withdrawn. Four substances are concerned by the initial grounds of concern "Endocrine disruptor" : methyl N-{[dimethoxy(methyl)silyl]methyl}carbamate ; 4-(4-isopropoxyphenylsulfonyl)phenol ; 4,4'-Isopropylidenediphenol, ethoxylated ; Esterification products of 1,3-dioxo-2-benzofuran_5-carboxylic acid with nonan-1-ol
https://echa.europa.eu/documents/10162/879660/draft_corap_update_2026-2028_en.pdf/01102836-365a-4215-6027-9562c4460235

EDLists - List Updates,
(décembre 2025),
List I
Medetomidine added to list I: BPC ED opinion has now been legally adopted
Flufenacet added to list I: EFSA ED opinion has now been legally adopted
List II
Diisopentyl phthalate; di-n-pentyl phthalate; 1,2-benzenedicarboxylic acid, dipentyl ester, branched and linear; n-pentyl-isopentyl phthalate added: ED HH and ENV CLH intention submitted
α-cyano-3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (Cypermethrin) added: ED HH and ENV CLH intention submitted
Chloroethane added: ED HH a CLH intention submitted
Potassium chlorate added: ED HH and ENV CLH intention submitted
The entry Mono- and di-phthalate esters with linear and/or branched alkyl moieties with at least one longest continuous c chain counted from the ester function corresponding to C4-C6 and/or w C6 cyclic saturated c chains and/or w unsaturated hydrocarbyl moieties changed named to: Mono- and di-ortho-phthalate esters with at least one of the following: a linear or branched alkyl moiety with a C4-C6 backbone with possible substitution by methyl and/or ethyl groups; a benzyl moiety with methylene possibly substituted by methyl and/or ethyl groups; a cyclopentyl or cyclohexyl moiety with possible substitution by methyl and/or ethyl groups [*The backbone is defined as the longest linear carbon chain from the ester function]*
Butanoic acid, 4-amino-4-oxosulfo-, N-coco alkyl derivs., monosodium salts, compds. with triethanolamine removed: REACH substance evaluation concluded. ED concern unresolved
4,4'-(1,3-phenylene-bis(1-methylethylidene))bisphenol removed: REACH substance evaluation concluded. ED concern unresolved
Benzophenone-5 removed: SCCS evaluation finalized.
Benzophenone-2 removed: SCCS evalution finalized (added to list III)
Medetomidine removed: Added to list I
Flufenacet removed: Added to list I
List III
Oxybenzone (Benzophenone-3; BP-3) added by Denmark
4,4'-isopropylidenedi-2,6-xylol (TMBPA) added by Denmark
Reaction products of phosphoryl trichloride and 2-methyloxirane (TCPP) added by Denmark
Tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP) added by Denmark

Phenol, methylstyrenated added by Denmark
Benzophenone-2 added by Denmark https://edlists.org/list-updates

« En déréglementant les pesticides chimiques, la Commission européenne ferait reculer l'Europe de trente ans »,
Le Monde (décembre 2025),
Un collectif de 114 organisations de protection de l'environnement, sous la houlette de Nadine Lauverjat, déléguée générale de Générations futures, demande, dans une tribune au « Monde », le retrait immédiat de la proposition de Bruxelles d'autoriser la plupart des pesticides de façon illimitée. https://www.lemonde.fr/idees/article/2025/12/01/en-dereglementant-les-pesticides-chimiques-la-commission-europeenne-ferait-reculer-l-europe-de-trente-ans_6655514_3232.html

Fluorure de sodium : proposition de classement comme perturbateur endocrinien et toxique pour la reproduction,
(18 décembre 2025),
Suite à des évaluations menées dans le cadre du règlement CLP (classification, étiquetage et emballage des produits), l'Anses propose de classer le fluorure de sodium comme perturbateur endocrinien pour la santé humaine (catégorie 1) et substance toxique pour la reproduction (catégorie 1B). Le dossier scientifique est en consultation publique sur le site de l'Agence européenne des produits chimiques (ECHA) jusqu'au 16 janvier 2026.
https://www.anses.fr/fr/content/fluorure-de-sodium-proposition-de-classement-comme-perturbateur-endocrinien-et-toxique-pour

PFAS : vers une surveillance élargie,
ANSES (octobre 2025),
Restreindre l'utilisation des composés per- et polyfluoroalkylées (PFAS) est une priorité pour limiter leurs émissions dans l'environnement et les pollutions qui en découlent. Face à une famille de substances aussi vaste et hétérogène, identifier les plus préoccupantes est un élément majeur pour optimiser les dispositifs de surveillance. Pour la première fois, l'Anses a compilé et exploité les données de contamination disponibles dans l'ensemble des milieux de l'environnement, l'alimentation, les produits de consommation et la biosurveillance, etc. en France. A l'issue de ce travail, l'Anses dresse un état des lieux de la contamination par les PFAS et propose des stratégies de surveillance adaptées à ces substances. https://www.anses.fr/fr/content/surveillance-nationale-des-PFAS-integrer-les-donnees-de-contamination-et-de-toxicite

PFAS : les résultats de la campagne nationale de mesure dans l'eau destinée à la consommation,
ANSES (décembre 2025),
La campagne nationale de mesure des composés émergents dans l'eau potable menée par l'Anses de 2023 à 2025 s'est intéressée aux PFAS. La présence de substances appartenant à ce vaste groupe restait en effet jusqu'à présent insuffisamment documentée dans l'eau destinée à la consommation humaine. Sur les 35 PFAS recherchés, 20 ont été détectés dans des échantillons d'eau brute et 19 dans les échantillons d'eau distribuée au robinet. Certains ne sont présents que dans un seul prélèvement, tandis que d'autres sont plus fréquemment retrouvés, notamment le TFA, détecté dans 92 % des prélèvements d'eau distribuée comme d'eau brute. Les résultats de la campagne montrent que les concentrations des substances PFAS mesurées dans la grande majorité des prélèvements analysés sont inférieures aux limites règlementaires lorsqu'elles leur sont applicables.
https://www.anses.fr/fr/content/pfas-les-resultats-de-la-campagne-nationale-de-mesure-dans-leau-destinee-la-consommation

Science seminar: Endocrine disruption activity of selected BPA alternatives,
(25 novembre 2025),
Our latest science seminar with Dr Sabrina Tait from the Italian National Institute of Health and Dr Antonio De la Vieja from the Spanish Carlos III Health Institute is now available on our science web pages and on our YouTube channel.
The seminar presents the preliminary results from a comparative analysis of endocrine-disrupting activity of selected BPA alternatives, generated under the Partnership for the Assessment of Risks from Chemicals (PARC). The seminar also provides initial discussion on how those results could be used for regulatory purposes under ECHA's mandate.
https://www.youtube.com/watch?v=zK3QVUv03VQ&list=PLOPGDACSd6qwL9t-vsr74mmcXdmc9qFes&index=8

PerturbAction : Le premier journal du CIAPE pour démystifier les perturbateurs endocriniens,
(6 janvier 2026),
Le Comité de la relève du CIAPE a franchi une étape majeure avec la parution de la première édition du journal PerturbAction, le 5 décembre 2025, lors du symposium annuel. Cette édition spéciale a été conçue pour marquer les 5 ans du CIAPE, une occasion unique de célébrer notre histoire et nos réalisations tout en lançant un projet novateur.
Objectif du journal :
PerturbAction vise à démystifier les perturbateurs endocriniens (PE) et à rendre l'information scientifique accessible à un public scientifique non expert des PE, tout en favorisant les échanges entre disciplines et générations. https://www.ciape-iceda.ca/perturbaction-le-premier-journal-du-ciape-pour-demystifier-les-perturbateurs-endocriniens/

EndoCompass Project: Environmental Endocrinology,
Andersson, A. M., Cianfarani, S., Köhrle, J., Main, K. M., Parent, A. S., Peeters, R., Reincke, M., Saravinovska, K. and Street, M. E., *Hormone Research in Paediatrics*, Dec 2025, Vol. 98, no. SUPPL 2, p. 163-186.

Background: Endocrine science remains underrepresented in European Union research programmes despite the fundamental role of hormone health in human well-being. Analysis of the CORDIS database reveals a persistent gap between the societal impact of endocrine disorders and their research prioritization. At national funding level, endocrine societies report limited or little attention of national research funding towards endocrinology. The EndoCompass project - a joint initiative between the European Society of Endocrinology and the European Society of Paediatric Endocrinology, aimed to identify and promote strategic research priorities in endocrine science to address critical hormone-related health challenges. Methods: Research priorities were established through a comprehensive analysis of the EU CORDIS database covering the Horizon 2020 framework period (2014-2020). An expert analysis was conducted by leading researchers in environmental endocrinology, integrating literature review, epidemiological evidence, and emerging research priorities to identify key challenges and opportunities across endocrine systems. Results: Research priorities span 5 critical domains: mechanisms and biomarkers of endocrine-disrupting chemical (EDC) actions; environmental pharmaceutical contamination; climate change effects on endocrine function; endocrine consequences of air and water pollution; and mechanisms linking environmental stress to hormone disruption. Special emphasis is placed on understanding developmental programming, transgenerational effects, and implications for public health policy. Conclusions: This component of the EndoCompass project provides an evidence-based roadmap for strategic research investment. The analysis demonstrates that environmental factors like EDCs fundamentally impact multiple endocrine systems, requiring coordinated research approaches. The findings support the

broader EndoCompass objective of aligning research funding with areas of highest potential impact in endocrine health. https://doi.org/10.1159/000549151

Scientific and Regulatory Perspectives on Chemical Risk Assessment of Pesticides in the European Union,
Buonsenso, F., *Journal of Xenobiotics*, Oct 21 2025, Vol. 15, no. 5.

People are exposed to pesticides daily through food, drinking water, and the environment, both in urban and rural settings. These chemicals, while offering economic and agricultural benefits through pest control and increased productivity, may pose a growing risk to human health and ecosystem biodiversity. While the European regulatory framework offers a robust foundation for risk assessment, significant limitations persist, especially in addressing cumulative exposure, low-dose effects, and chemical mixtures. This review focuses on selected scientific and regulatory challenges by reviewing recent European Food Safety Authority (EFSA) conclusions, Organization for Economic Co-operation and Development (OECD) test guidelines updates, and current European legislative approaches. Particular attention is given to the regulation of endocrine-disrupting and reprotoxic substances, highlighting progress and remaining gaps in implementation. A brief mention will also be made of immuno-toxic substances, for which no specific hazard class has yet been established. Building on official reports and peer-reviewed literature, this review provides a structured evaluation of the scientific and regulatory landscape, including underexplored issues like the transition to animal-free toxicology and integration of biomonitoring with health data. The goal is to propose realistic, evidence-based improvements to current frameworks using integrated, interdisciplinary approaches that connect toxicology, policy, and implementation science. A shift to a holistic, systems-based, and precautionary paradigm is vital to address emerging challenges and ensure strong protection of health and environment, as well as supporting the needs of the agricultural sector. https://doi.org/10.3390/jox15050173

Hazard identification and characterization of leachable chemicals from plastic products - a new PARC project,
Dirven, H., Bogusz, A., Bouwmeester, H., Busch, M., Duflos, G., Eriksen, G. S., Fardilha, M., Flores-Gomez, D., Franko, N., Gaté, L., Guichard, Y., Silva, M. J., Kamstra, J. H., Kasiotis, K. M., Kim, S., Kim, Y. J., Kim, Y., Van Der Koogh, E., Loureiro, S., Louro, H., Machera, K., Pieters, R. H. H., Spyropoulou, A., Tzanetou, E. N., Malheiro, C., Ravnjak, T., Repetto, G., Rivière, G., Ryu, C. S., Papadopoulou, E. A., Aliferis, K. A., Solhaug, A., Dolenc, M. S., Štampar, M., Tavares, A. M., Tollefsen, K. E., Ventura, C., Walkowiak, R., Zobl, W., Žegura, B., Snapkow, I. and Herzke, D., *Front Toxicol*, 2025, Vol. 7, p. 1719035.

A recent study has suggested that plastics may contain more than 16,000 chemicals, including additives, processing aids, starting substances, intermediates and Non-Intentionally Added Substances. Plastic chemicals are released throughout the plastic life cycle, from production, use, disposal and recycling. Most of these chemicals have not been studied for potential hazardous properties for humans and in the environment. To refine the risk assessment of these leachable chemicals, additional hazard data are needed. The PlasticLeach project within the EU co-funded Partnership for the Assessment of Risks from Chemicals (PARC) aims to address this data gap by screening several plastic products in daily use. Leachates will be prepared from a number of these plastic items, and these chemical mixtures will be further tested using several test guideline compliant assays and New Approach Methodologies covering both human health and environmental endpoints. The most toxic leachates will be characterized using a non-targeted analysis pipeline to identify chemicals in the leachate. When single chemicals of concern are identified, these will be further tested to determine hazardous properties and identify the respective

potency factors to better understand their specific hazard profiles. A tiered approach for hazard testing will be followed. The experimental work will be complemented by in silico toxicological profiling, using publicly available toxicity databases and tools, including Artificial Intelligence tools that cover both human and environmental endpoints. A comprehensive array of endpoints, including cytotoxicity, endocrine disruption, genotoxicity, immunotoxicity, reproductive toxicity and effects related to ecotoxicity will be evaluated. In this paper, we outline the plastic products to be tested and the battery of assays that will be used to identify hazards relevant to both human health and the environment. Data generated from in silico, in vitro, and in vivo approaches will be reported using standardized formats, stored within a centralized repository, and harmonized to adhere to the FAIR data principles (Findable, Accessible, Interoperable, and Reusable). This integrated strategy will not only advance our understanding of the risks associated with plastic-derived chemicals but will also provide critical support for regulatory decision-making and facilitate the development of safer, and more ecofriendly plastic materials in the future. https://doi.org/10.3389/ftox.2025.1719035

Perturbateurs endocriniens et grossesse : risques pour l'enfant et valeurs seuils sans effet ?,
F., G.-T., *Références en santé au travail Vos questions-nos réponses , INRS*, décembre 2025, no. 184, p. 3.

Un médecin du travail s'interroge sur les risques pour les enfants à naître de l'exposition professionnelle de leur mère aux perturbateurs endocriniens (PE), en particulier au bisphénol A (BPA) et aux phtalates, et sur l'existence de valeurs seuils sans effet.
https://www.inrs.fr/media.html?refINRS=QR%20190

Une démarche préventive indispensable face au rôle des perturbateurs endocriniens dans la survenue de cancers,
Fervers, B. and Amadou, A., *Actualités Pharmaceutiques*, 2026/01/01/ 2026, Vol. 65, no. 652, p. 28-31.

Les perturbateurs endocriniens (PE) sont suspectés d'augmenter le risque de plusieurs cancers (sein, prostate, testicule, thyroïde, endomètre, ovaires, pancréas, hémopathies malignes). La diversité des substances et l'accumulation des preuves scientifiques concernant les effets des faibles doses pendant des périodes critiques, les mécanismes multiples et les interactions entre PE, restreignent le champ du doute et soulignent l'importance d'une prévention à tous les niveaux. A necessary preventive measure given the role of endocrine disruptors in the development of cancer Endocrine disruptors (EDs) are suspected of increasing the risk of several cancers (breast, prostate, testicular, thyroid, endometrial, ovarian, pancreatic, and malignant blood disorders). The diversity of substances and the accumulation of scientific evidence concerning the effects of low doses during critical periods, multiple mechanisms, and interactions between EDCs limit the scope for doubt and underscore the importance of prevention at all levels. https://doi.org/10.1016/j.actpha.2025.10.012

What do people need to know about endocrine disrupting chemicals and health? A mental models approach using focus groups of community-engaged research teams and a national survey,
Boronow, K. E. and Brody, J. G., *BMC Public Health*, Nov 22 2025, Vol. 25, no. 1, p. 4414.

BACKGROUND: Endocrine disrupting chemicals (EDCs), which interfere with the body's natural hormones, are ubiquitous in everyday environments and consumer products. Nearly everyone is routinely exposed, and growing evidence links them to adverse health outcomes including cancers, impaired fertility, metabolic disorders, and neurodevelopmental effects. Major medical and scientific groups recommend exposure reduction. To make informed decisions about individual- and

societal-level exposures to EDCs, people need relevant knowledge. Knowledge is one component of environmental health literacy, a multidimensional concept supporting readiness to protect health from environmental risks. This study sought to develop expert consensus about communications targets for EDCs and to learn how public knowledge matches these targets. METHODS: We convened focus groups with community-engaged research teams (n = 38) to define targets for public understanding. We coded transcripts, mapped causal pathways influencing EDC exposures and health outcomes using a mental models approach, and identified communication priorities. We then fielded a quantitative online survey among adults living in the U.S. (n = 504) to compare their knowledge with the mental model. We computed response frequencies and used multiple regression to evaluate associations between a knowledge index and participant characteristics. RESULTS: Focus group participants highlighted that people need to know that EDCs affect nearly all systems in the human body and that scientific evidence supports limiting exposure. They emphasized that policy controls can be more effective than personal action at reducing exposure, and that current U.S. chemicals regulations are not protective. Survey respondents were generally aware that EDCs can affect fertility, cancer, and child brain development (84-90%, n = 426-452), and they had some understanding of exposure pathways (58-86%, n = 295-435). However, most participants had large knowledge gaps about U.S. chemicals regulation and wrongly believed that chemicals must be safety-tested before being used in products (82%, n = 414), that product ingredients must be disclosed (73%, n = 368), and that restricted chemicals cannot be replaced by similar substitutes (63%, n = 317). CONCLUSIONS: U.S. adults typically understood that EDCs affect health. However, incomplete information about how people get exposed to EDCs and misconceptions about U.S. chemicals regulations limit appropriate actions. These knowledge gaps are targets for future communications about EDCs and harmful chemicals more broadly. https://doi.org/10.1186/s12889-025-25561-4

Integrative assessment of endocrine disruption: From in vitro mechanisms to species extrapolation - Highlights of the German Pharma-Tox Summit 2025,
Haßmann, U., Gölz, L., Geci, R., Stefanidis, K., Brandt, J. L., North, E., Feiertag, K., Schopfer, C. R., Amann, S., Melching-Kollmuss, S. and Landsiedel, R., *Toxicology*, Feb 2026, Vol. 520, p. 154370.

Endocrine-disrupting chemicals (EDCs) are a growing focus in human and environmental risk assessment, as reflected by the new EU CLP hazard classes for endocrine disruptors. Within this context, the symposium "Cross-Species Extrapolation in Endocrine Disruption Assessments" was held at the 10th German Pharm-Tox Summit (GPTS) 2025 in Hannover (March 11-13), which formed part of the 91st annual meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology (DGPT). The symposium assembled diverse lines of research addressing endocrine disruption from complementary angles. Contributions ranged from advanced experimental model systems, such as refined zebrafish embryo assays for thyroid hormone disruption, to high-throughput in silico and in vitro-based kinetic modelling frameworks that support quantitative in vitro to in vivo extrapolation and AOP-informed risk assessment. Clinical and translational perspectives were added by targeted LC-MS/MS profiling of steroid conjugates as biomarkers for adrenal tumours. Further talks expanded the mechanistic toolbox for thyroid disruption, including enzyme- and protein-binding-based in vitro assays, and highlighted metabolic endocrine disruptors that act beyond the EATS (estrogen, androgen, thyroid and steroidogenesis) pathways. A regulatory-oriented analysis of thyroid-related modes of action across vertebrate taxa underscored the importance of clearly defining domains of applicability for cross-species extrapolation. At the same time, the discussions revealed critical gaps, including still limited taxonomic applicability domains, incomplete regulatory coverage beyond established endocrine pathways and limited transparency in predictive tools. Together, these contributions illustrate how integrated

experimental, computational and regulatory science can advance mechanism-based, animal-reduced assessment of endocrine disruptors. https://doi.org/10.1016/j.tox.2025.154370

Special Issue "Progress in Research on Endocrine-Disrupting Chemicals", Kitraki, E., *International Journal of Molecular Sciences*, 2026, Vol. 27, no. 1, p. 39. https://www.mdpi.com/1422-0067/27/1/39

Safe-and-sustainable-by-design approach to polyesters from non-oestrogenic bisphenols, Margarita, C., Pierozan, P., Subramaniyan, S., Shatskiy, A., Pakarinen, D., Fritz, A., Lundqvist, E., Chu, V., Hagelin, H., Norinder, U., Hakkarainen, M., Karlsson, O. and Lundberg, H., *Nature Sustainability*, 2025.

Most contemporary chemical processes rely on non-renewable resources and reagents associated with negative impact on environment and human health. As a result, the safe-and-sustainable-by-design (SSbD) framework is launched to guide the innovation towards safe and sustainable materials and chemical products. Bisphenol A (BPA) is a widely used chemical in the production of plastics but known to activate oestrogen receptors and linked by numerous studies to adverse effects on both human health and the environment. Here we demonstrate how SSbD can lead a multidisciplinary study for the identification of non-oestrogenic BPA analogues suitable for incorporation into high-performance polymeric materials. Toxicological evaluation of a library of 172 bisphenols using an in silico model identified 20 promising candidates that are synthesized from renewable lignin-sourced feedstocks via benign dehydrative catalytic routes. Subsequent in vitro assessment of their oestrogen receptor activity identifies bisguaiacol F as optimal BPA analogue, which is incorporated into a polyester with attractive thermal stability and flexibility. This work demonstrates an effective workflow for the discovery of renewable and non-oestrogenic bisphenols by taking advantage of the synergy of synthetic chemistry, toxicology and computational modelling. https://doi.org/10.1038/s41893-025-01672-z

EndoCompass Project: Research Roadmap for Diabetes, Obesity, and Metabolism, Mathieu, C., Meireles, M., Pagotto, U., Wabitsch, M., Banerjee, I., Bartolomé, A., Battelino, T., Beck, J., Chiarelli, F., De Leon, D. D., Dovc, K., El Goch, M., Galderisi, A., Gevers, E., Gillard, P., Haliloglu, B., Hoermann, H., Mankovsky, B., Mertens, J., Mohnike, K., Oram, R., Pasquini, T., Pearson, E., Pieber, T. R., Polovina, S., Raskin, J., Roeper, M., Ruck, L., Estebanez, M. S., Tankova, T., Thornton, P., Van Rossum, E. F. C., Vukovic, R., Worth, C. and Zachurzok, A., *Hormone Research in Paediatrics*, Dec 2025, Vol. 98, no. SUPPL 2, p. 60-90.

Background: Endocrine science remains underrepresented in European Union research programmes despite the fundamental role of hormone health in human well-being. Analysis of the CORDIS database reveals a persistent gap between the societal impact of endocrine disorders and their research prioritization. At the national funding level, endocrine societies report limited or little attention of national research funding towards endocrinology. The EndoCompass project - a joint initiative between the European Society of Endocrinology and the European Society of Paediatric Endocrinology, aimed to identify and promote strategic research priorities in endocrine science to address critical hormone-related health challenges. Methods: Research priorities were established through comprehensive analysis of the EU CORDIS database covering the Horizon 2020 framework period (2014-2020). Expert consultation was conducted to identify key research priorities, followed by broader stakeholder engagement including society members and patient advocacy groups. Results: Research priorities include genetic/epigenetic factors, brain-periphery communication, and environmental influences. Key therapeutic areas include innovative approaches for monogenic disorders, incretin mimetics, dual receptor agonists, microbiome analysis, and improved behavioural

interventions. For type 1 diabetes, priorities focus on early detection, insulin delivery systems, and disease-modifying therapies. Conclusions: This component of the EndoCompass project provides an evidence-based roadmap for strategic research investment. This framework identifies crucial investigation areas into diabetes and obesity pathophysiology, prevention, and treatment strategies, ultimately aimed at reducing the burden of metabolic disorders on individuals and society. The findings support the broader EndoCompass objective of aligning research funding with areas of highest potential impact on endocrine health. https://doi.org/10.1159/000549194

EndoCompass Project: Research Roadmap for Thyroid Endocrinology,
Piekielko-Witkowska, A., Elisei, R., Léger, J., Bendlováa, B., Pekova, B. B., Caron, P., Durante, C., Fassnacht, M., Feldt-Rasmussen, U., Nyström, H. F., Jansen, H., Köhrle, J., Kus, A., Ludgate, M., Mertens, J., Oczko-Wojciechowska, M., Peters, C., Schoenmakers, N., Stoupa, A., Van Santen, H., Trimboli, P., Van Trotsenburg, P. and Visser, W. E., *Hormone Research in Paediatrics*, Dec 2025, Vol. 98, no. SUPPL 2, p. 144-157.

Background: Endocrine science remains underrepresented in European Union research programs despite the fundamental role of hormone health in human well-being. Analysis of the CORDIS database reveals a persistent gap between the societal impact of endocrine disorders and their research prioritization. At national funding level, endocrine societies report limited or little attention of national research funding toward endocrinology. The EndoCompass project - a joint initiative between the European Society of Endocrinology and the European Society of Paediatric Endocrinology, aimed to identify and promote strategic research priorities in endocrine science to address critical hormone-related health challenges. Methods: Research priorities were established through comprehensive analysis of the EU CORDIS database covering the Horizon 2020 framework period (2014-2020). Expert consultation in thyroid endocrinology was conducted to identify key research priorities, followed by broader stakeholder engagement including society members and patient advocacy groups. Results: For thyroid disorders, research priorities encompass neoplastic and nonneoplastic conditions, focusing on disease mechanisms, improved diagnostics and treatments, and the impact of environmental and metabolic factors. Key areas include personalized medicine approaches, artificial intelligence applications, and the establishment of pan-European registries to advance understanding of rare thyroid conditions. Conclusions: The thyroid component of the EndoCompass project provides an evidence-based roadmap for strategic research investment. This framework identifies crucial investigation areas into thyroid disease pathophysiology, prevention, and treatment strategies, ultimately aimed at reducing the burden of thyroid disorders on individuals and society. The findings support the broader EndoCompass objective of aligning research funding with areas of highest potential impact in endocrine health.
https://doi.org/10.1159/000549075

L'exposition de la population pédiatrique aux perturbateurs endocriniens, une problématique de premier plan,
Portefaix, A., *Actualités Pharmaceutiques*, 2026/01/01/ 2026, Vol. 65, no. 652, p. 25-27.

L'exposition des plus jeunes aux perturbateurs endocriniens représente un réel défi, d'autant que les 1 000 premiers jours de vie, l'enfance et la puberté sont des périodes de grande vulnérabilité. La prévention repose sur la formation et l'information des professionnels et des familles. Exposure of the pediatric population to endocrine disruptors: a major issue Exposure of young children to endocrine disruptors poses a real challenge, especially since the first 1,000 days of life, childhood, and puberty are periods of great vulnerability. Prevention relies on training and informing professionals and families. https://doi.org/10.1016/j.actpha.2025.10.011

Breastfeeding in a Polluted World: Perspective on the Properties of Breast Milk and the Need for Protection,
Street, M. E., Shulhai, A. M., Fanos, V., Papini, A. M., Ponzi, D., Ragusa, A., Rollo, D. and Palanza, P., *Journal of Clinical Medicine*, Nov 13 2025, Vol. 14, no. 22.

Breast milk (BM) is a unique biological fluid that represents the optimal nutritional source for infants, uniquely adapted through millions of years of evolution. BM is not only a nutritional fluid but a dynamic biological system, evolved to provide optimal growth, immune protection, and neurodevelopmental support. Its unique composition-including macronutrients, micronutrients, bioactive molecules, and stem cells-makes it essential in early life. Breastfeeding further promotes psychological well-being, secure attachment, and maternal-infant bonding. Yet, in recent decades, concern has grown over environmental contaminants in BM, including endocrine-disrupting chemicals (EDCs) and micro/nanoplastics. These pollutants have the potential to disrupt endocrine signaling, neurodevelopment, metabolic programming, and immune development, thereby undermining the natural advantages of breastfeeding. Therefore, a better understanding of the unique features of BM, while investigating the effects of these contaminants, is important for safeguarding maternal and infant health. This perspective article highlights the current knowledge on BM and indicates the need for further research. It also emphasizes the need for appropriate public health measures aimed at reducing exposure to pollutants and lowering associated risks, as well as preventive strategies to protect breast milk and breastfeeding in such a changing environment, as it is uniquely designed to promote the health of children.
https://doi.org/10.3390/jcm14228034

A health conundrum of bisphenol A and its alternatives: charting a path beyond the structural analogue substitution pitfall,
Yang, X. and Yu, Y. X., *Journal of Environmental Exposure Assessment*, Sep 2025, Vol. 4, no. 3.

With the restriction of bisphenol A (BPA) in certain consumer products due to its endocrine-disrupting properties, structurally analogous alternatives such as bisphenol S (BPS) and bisphenol F (BPF) have rapidly entered the market. This shift has led to a wave of "regrettable substitutions"-chemicals that appear more environmentally friendly but may pose comparable or even unforeseen risks. Based on the latest toxicological evidence and population biomonitoring data, this perspective highlights that most mainstream BPA alternatives exhibit estrogenic/anti-androgenic activity, metabolic disruption potential, reproductive toxicity, and neurodevelopmental effects similar to those of BPA. Their widespread presence, environmental persistence, and hidden health hazards expose critical weaknesses in the current "like-for-like substitution" regulatory approach. To address this challenge, it is imperative to establish a safer assessment framework that integrates early endocrine disruption screening with exposome-based evaluation. Shifting from "hazard substitution" to a "functional safe-by-design" strategy is critical to circumvent the pitfalls of structural-analogue substitution, protect public health, and support sustainable development.
https://doi.org/10.20517/jeea.2025.39

Shaping the future of human biomonitoring (HBM): progress, strategy, and global vision from ISES Europe and the HBM Global Network,
Zare Jeddi, M., Hopf, N. B., Galea, K. S., Jones, K., Louro, H., Silva, M. J., Covaci, A., Santonen, T., Scheepers, P. T. J., Viegas, S., Quirós-Alcalá, L., Qureshi, A., Marder, M. E., Von Goetz, N., Kasiotis, K. M., Machera, K., Sepai, O., Duca, R. C., Ghosh, M., Van Nieuwenhuyse, A., Chung, M. K., Kil, J., Nakayama, S. F., Menouni, A., Chbihi, K., Vekic, A. M., Souza, G., Waras, M. N., Ali, I., Bader, M., Kumar, E., Makris, K. C., Lin, E. Z., Haynes, E. N., Ait Bamai, Y., Kwon, J. H., Huang, P. C. and Pasanen-Kase, R., *Environ Int*, Dec 7 2025, Vol. 207, p. 109985.

Human biomonitoring (HBM) continues to play an indispensable role within exposure science, offering insights into aggregate chemical exposures across populations and life stages. Since 2018, the European chapter of the International Society of Exposure Science Human Biomonitoring Working Group (ISES Europe HBM WG) has aimed to facilitate generation of more and high-quality HBM data. The working group aims to strengthen integration of HBM data into regulatory frameworks through improved study design, harmonized methodologies, and enhanced reporting practices. Key achievements in the past seven years include the harmonization of HBM metadata through development of minimum information requirements for HBM (MIR-HBM), development of chemical-specific BASIC Guides for occupational health and hygiene professionals, and establishment of the FAIR (Findable, Accessible, Interoperable, and Reusable) Environmental and Health Registry (FAIREHR) to enhance data transparency and reusability. Recognizing the need for broader impact, the HBM Global Network was launched in 2025 to promote worldwide collaboration, capacity building, and policy integration. Together, ISES Europe HBM WG and the HBM Global Network form a coordinated platform with shared governance, strategic priorities, and digital infrastructure. This short communication outlines the progress to date, strategic pillars guiding our work, and ongoing initiatives linking science, policy, and practice. We call on researchers, regulators, and stakeholders worldwide to join these networks, strengthen harmonized approaches, and ensure that HBM becomes a cornerstone of 21st-century chemical risk governance. https://doi.org/10.1016/j.envint.2025.109985

Flame retardant biomarker changes with furniture replacement after flammability standard update,
Attfield, K. R., Berger, K., Dodson, R. E., Bennett, D. H., Rodgers, K. M., Moran, R., Stoiber, T., Wang, Y., Gao, S., Smith, S. C., Park, J. S., Blum, A. and Wu, N., *Environ Pollut*, Feb 1 2026, Vol. 390, p. 127326.

Upholstered furniture has been a major source of flame retardant (FR) exposures in the United States. However, the California update to furniture flammability standards has allowed compliance without relying on chemical additives. We investigated whether FR biomarkers would decrease in participants who replaced furniture foam or upholstered furniture with items manufactured after the policy change. Building off previous work demonstrating decreased dust FR concentrations after furniture replacement, we collected urine and blood from 25 participants prior to furniture replacement and approximately one year after and from a comparison group (n = 28) over a similar time frame. Serum was analyzed for 19 polybrominated diphenyl ethers (PBDEs) and urine for 3 metabolites of organophosphate FRs (OPFRs). For BDE-47, BDE-99, and BDE-100, time to decline by half was 1.9-3.9 times longer in the comparison group than the replacement group (equivalent to 1.4 years (median) in the replacement group versus 2.6-5.2 years in the comparison group). For BDE-153, times to decline by half were not significantly different. For OPFR metabolites, which are excreted within days after exposure, concentration changes were much more variable. Nonsignificant greater decreases were seen for bis(1,3-dichloroisopropyl) phosphate in the replacement group and for diphenyl phosphate in the comparison group, whereas concentrations remained level or increased for bis(2-chloroethyl) phosphate. Moderate positive correlations were observed for baseline PBDE concentrations with baseline dust concentrations (ρ = 0.58-0.60); OPFRs were less correlated. Magnitudes of change were mostly positively correlated between dust and biomarker concentrations but not significant. Overall, results indicate that updated flammability standards can reduce FR exposures. https://doi.org/10.1016/j.envpol.2025.127326

Reference values and exposure risk of bisphenol A and its substitutes in Taiwan: Taiwan environmental survey for Toxicants (TESTs) 2013-2016,
Chen, H. C., Chang, J. W., Lin, Y. J., Chang, W. T., Huang, H., Chen, C. Y. and Huang, P. C., *Ecotoxicology and Environmental Safety*, Nov 15 2025, Vol. 307.

Background: Exposure to bisphenol A (BPA) and its substitutes bisphenol F (BPF) and bisphenol S (BPS) poses potential health concern. Following the European Food Safety Authority's 2023 re-assessment of tolerable daily intake for BPA, the exposure risks and reference values of these bisphenols in Taiwan remain unclear. This study aimed to establish the human urinary reference values of BPA and its substitutes and identify exposure-related risk factors using biomonitoring data. Methods: We analyzed urinary BPA, BPF and BPS in 1964 participants from the Taiwan Environmental Survey for Toxicants (TEST 2013-2016), covering major regions and age groups of the Taiwanese population, and stratified by sex and age (7-11, 12-17, 18-39, 40-64, and >= 65 years). Urinary bisphenol concentrations were quantified using ultraperformance liquid chromatography tandem mass spectrometry. Results: Bisphenol levels were significantly associated with personal care product use, diet, medication, and plastic use (p < 0.001). BPF showed the highest median levels (8.09 mu g/g creatinine), followed by BPA (7.71 mu g/g creatinine) and BPS (1.93 mu g/g creatinine). Adults exhibited significantly higher concentrations of BPA and its substitutes than minors (BPA: 8.89 vs. 5.80; BPF:9.06 vs. 6.32; BPS: 2.18 vs.1.50 mu g/g creatinine), with women showing higher BPs levels than men. Bisphenol levels increased with age, peaking in individuals aged >= 65 years. Daily intake was highest for BPF across all age groups, exceeding that of BPA and BPS. In contrast, estimated DI and hazard index (HI) were higher among minors than adults (BPA DI: 2.61 vs. 2.15; BPF DI: 2.84 vs. 2.19; BPS DI: 0.71 vs. 0.53 ng/kg bw/day). Using the EFSA 2023 tolerable daily intake (TDI), hazard quotient and index exceeded 1 across all groups, indicating potential health concern. Conclusion: Taiwanese residents are exposed to BPA and its substitutes, with women and minors, being at an increased risk of exposure. The findings highlight the need for continued biomonitoring and risk evaluation of bisphenol substitutes to inform evidence-based exposure reduction strategies. https://doi.org/10.1016/j.ecoenv.2025.119401

Detection of Endocrine Disruptors in Human Placenta: A Pilot Study on Exposure and Histopathological Findings,
Robalo, M., Ayraud-Thévenot, S., Migeot, V., Gourgues, A. S., Albouy, M. and Venisse, N., *Ther Drug Monit*, Dec 9 2025.

BACKGROUND: Endocrine-disrupting chemicals (EDCs), such as bisphenols and parabens, are widely used in consumer products and can interfere with placental development. Although their cellular and molecular effects have been explored, the relationship between these factors and placental anatomical abnormalities remains unclear. This pilot study assessed histopathological lesions in human placentas and evaluated potential associations with varying bisphenol and paraben concentrations measured in placental tissue. METHODS: Thirty-seven placentas from the Pregnancy Prevention Endocrine Disruptors cohort were analyzed. Histological assessments were conducted according to standardized protocols, which included evaluating chronic villitis of unknown etiology, intervillitis, chorangiosis, and placental trophicity. Bisphenols (bisphenol A, bisphenol S, bisphenol F, and chlorinated bisphenol A derivatives) and parabens (methyl-, ethyl-, propyl-, and butyl-paraben) were assessed using liquid chromatography coupled to tandem mass spectrometry. RESULTS: EDCs were frequently detected in placental tissue. Villitis of unknown etiology lesions were identified in 16% of placentas; however, high-grade forms were rare. Chorangiosis was observed in 36% of placentas, and 38% showed hypertrophy. No significant associations were observed between EDCs and specific placental lesions; however, these trends may represent an exploratory signal that warrants further investigation. CONCLUSIONS: This study confirms widespread maternal exposure

to EDCs and demonstrates the feasibility of directly detecting these compounds in placental tissue. Although no conclusive association was found between EDC exposure and placental lesions, further research with larger cohorts is warranted to explore potential mechanistic relationships. https://doi.org/10.1097/ftd.0000000000001414

Evaluation of the efficacy of PREVENIR (PREVention ENvIronment Reproduction) platforms on urinary markers of chemical exposure in pregnant women: protocol for an unblinded randomised clinical trial (PREVENIR-G),
Delva, F., Sentilhes, L., Francis-Oliviero, F., Bessonneau, V., Sunyach, C., Audouin, C., Paris, C., Haddad, B., Matrat, M., Pairon, J. C., Belacel, M., Sitta, R., Roberts, T., Bretelle, F. and Garlantezec, R., *Bmj Open*, Nov 9 2025, Vol. 15, no. 11.

Introduction It has been reported that pregnant women used more cosmetics daily than non-pregnant women. Phenoxyacetic acid is the main metabolite of phenoxyethanol, the most frequent preservative in cosmetics used in Europe, previously associated with reproductive effects (longer time to conception, endocrine disruptors in newborns and poorer verbal comprehension in children). In France, specialised platforms (PREVention ENvIronment Reproduction (PREVENIR)) in university hospital maternity wards are dedicated to evaluating environmental and occupational exposures in patients with pregnancy-related pathologies and supporting targeted prevention efforts. These platforms are composed of occupational health physicians, obstetrician-gynaecologists, midwives, occupational health nurses, and occupational health and environmental engineers. To assess the efficacy of these platforms, we developed a randomised clinical trial, the protocol for which is presented in this paper. The primary objective of the PREVENIR-G Study is to compare the change in urinary phenoxyacetic acid concentrations from baseline to 3 months postintervention between an intervention group and a control group. To date, the intervention has been integrated into routine care in certain facilities; however, its efficacy remains unproven. It is therefore essential to assess the relevance of this intervention, considering both its potential benefits and any adverse effects, such as increased stress or anxiety.Methods and analysis This study is an unblinded, randomised clinical superiority trial with two parallel groups (intervention vs no intervention) in four university maternity hospitals in France. We will include 300 pregnant women (aged 18 years or older) who are under 24 weeks of gestation (150 per group) referred to the participating PREVENIR platforms for management. The intervention will consist of clinical prevention management through the PREVENIR platforms, involving a consultation with an environmental health expert for an assessment of environmental and occupational exposures. During the consultation, targeted prevention messages will be provided based on identified exposures. The no intervention comparator will be a waiting-list control group. At the inclusion visit, patients will receive urine collection vials for samples to be collected at baseline and again at 3 months. Urine samples will be collected twice in a single day, on three separate days, during the collection week at home. In the week following the urine collection period, only participants in the intervention group will engage with the PREVENIR platforms. The primary outcome will be the difference in the urinary phenoxyacetic acid concentration between baseline and 3 months postintervention, compared between the intervention and control groups.Ethics and dissemination The study has been approved by the hospital ethics committee (CCP Ouest 2, no. 2023-A00941-44). All participants will provide written informed consent. Results will be shared through presentations and publications.Trial registration number NCT06642818 https://doi.org/10.1136/bmjopen-2024-097795

Endocrine Disrupting Chemicals in Human Milk: A Systematic Review of Concentrations and Potential Health Implications,
Dunn, F., Sullivan, H., Romano, M., Chambers, C. D., Braun, J. M. and Manz, K. E., *Current Environmental Health Reports*, Nov 25 2025, Vol. 12, no. 1.

Purpose of Review Endocrine-disrupting chemicals (EDCs) disrupt the synthesis, transport, action, or metabolism of endogenous hormones in the human body. EDCs often enter the body through inhalation, ingestion, or dermal contact and can accumulate in the body. Remobilization or transfer of EDCs can occur during lactation, causing human milk to become contaminated with a variety of EDCs, which could expose nursing infants and children to these chemicals. Recent Findings Several studies have examined the concentration ranges for one or multiple EDC(s) in human milk. Additional studies document associations between EDC exposure and adverse health outcomes, many of which are in adult populations. It is therefore essential to understand the extent to which EDCs in human milk contribute to cumulative early-life exposures. Summary We performed a literature review of peer-reviewed studies reporting concentrations of one or more of the following EDCs in human milk during or after 2004: bisphenols, organochlorine pesticides (OCPs), polycyclic aromatic hydrocarbons (PAHs), parabens, polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), per- and polyfluoroalkyl substances (PFAS), and phthalates. We identified concentration ranges for each chemical detected in human milk and health impacts associated with early-life exposures to EDCs noted across studies from this review. Determining the presence of EDCs in human milk and the associated effects of exposure through nursing is essential to develop feeding recommendations that safeguard infant and child health. https://doi.org/10.1007/s40572-025-00515-5

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., Neal, M. S., Foster, W. G. and Feng, Y. L., *ACS Meas Sci Au*, Dec 17 2025, Vol. 5, no. 6, p. 790-804.

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

Toxicité sur les animaux

Biochemical and histopathological investigation to study the impact of pyriproxyfen exposure on ovarian morphology and reproductive function in female rats,
Ali, S., David, M., Fatima, J., Afaqi, H., Jahan, S., Afsar, T., Disi, D. A., Husain, F. M., Amor, H. and Razak, S., *Bmc Pharmacology & Toxicology*, Nov 12 2025, Vol. 26, no. 1.

Background Pyriproxyfen (PYR) is a pyridine-based broad-spectrum insect growth regulator and pesticide which works as an analogue of juvenile hormone. Its exposure to aquatic animals and crops is linked with various hazardous effects on biological functions. We aimed to find the possible reprotoxic effects of pyriproxyfen in adult female Sprague-Dawley rats through histological and biochemical approaches. Methods Adult female rats were assigned to four groups and were administered 0 mg/kg (Control), 62 mg/kg b.w, 124 mg/kg b.w, and 186 mg/kg b.w., of PYR dissolved in distilled water for 28 consecutive days. Body mass index, blood glucose levels, total protein concentration, lipid profile, ovarian histology and reproductive hormonal profiles were determined. Results There were no significant changes in body weight due to PYR exposure; however, slight alterations in ovarian and uterine weights were noted in the treatment groups. The 186 mg/kg b.w. treatment significantly affected estrous cyclicity. Furthermore, a non-significant increase in total protein levels and a significant ($p < 0.05$) rise in triglyceride and total cholesterol levels were recorded. However, a significant decline in high-density lipids was recorded in the high-dose treatment group (186 mg/kg bw) as compared to the control. A notable reduction in plasma concentration of estradiol, progesterone, and cortisol levels was recorded between the control and all the treated groups. Ovarian histomorphological analysis showed distorted basal membranes, increased empty spaces, tissue decompaction, degenerate follicles, and disassembled epithelium in the high-dose treated group (186 mg/kg b.w). Conclusion Oral administration of PYR in adult female rats leads to altered organ weights, disturbed normal estrous cycle, increased triglycerides and total cholesterol, reduced high-density lipids concentrations, and damaged ovarian architecture, affecting biochemical and reproductive function in female rats. https://doi.org/10.1186/s40360-025-01045-4

The Effect of Oral Administration of Bisphenol A and AF on Their Deposition in the Body Organs of Growing Pigs and the Relationship to Growth Rate,
Bahelka, I., Stupka, R., Zadinová, K., Sprysl, M. and Cítek, J., *Animals*, Nov 5 2025, Vol. 15, no. 21.

Bisphenol A (BPA) and its analogues, such as bisphenol AF (BPAF), are widely used mainly in the plastic industry. These compounds can leach into the environment and negatively impact living organisms, including farm animals such as pigs. The aim of the study was to evaluate concentrations of BPA and BPAF in plasma and tissues of pigs after oral administration at a lower-20 mu g (10 mu g BPA + 10 mu g BPAF)/kg body weight (b.w.)/day-and higher dose-60 mu g (30 mu g BPA + 30 mu g BPAF)/kg b.w./day-for 21 days. The concentrations of BPA and BPAF in plasma and liver were monitored immediately after finishing the bisphenols administration, as well as two and four weeks after that. Generally, pigs receiving higher doses of BPA/BPAF showed the highest levels across most parameters, followed by those with lower doses and the control group. Results showed that both bisphenols remained in the organs of experimental pigs for two and four weeks after the administration was completed, respectively. Results also showed that the growth rate did not have a significant effect on the accumulation of bisphenols in pig tissues. The results of the present study have shown that oral administration of bisphenols led to an increase in the concentration of BPA and BPAF in plasma and other tissues of young pigs. Moreover, the fact that both BPA and BPAF were also detected in control pigs suggests that the farm environment was contaminated with these substances. This may pose a risk not only to the health and performance of pigs but also to human health, through the consumption of pig organs. https://doi.org/10.3390/ani15213214

The assessment for potential thyroid-mediated endocrine disruption in amphibians: Clarification on the use of new methods and on the interpretation of changes in thyroid histology,
Baumann, L., Baynes, A., Bennekou, S. H., Crofton, K., Dang, Z., Degitz, S., Fini, J. B., Gilbert, M., Holbech, H., Terron, A., Van Duursen, M., Mcvey, E., Arena, M., Kienzler, A., Rizzuto, S., Bouza, L. V. and Wilks, M., *Efsa j*, Dec 2025, Vol. 23, no. 12, p. e9815.

Amphibians (specifically Xenopus laevis) are used as the model species to assess potential endocrine-disrupting properties in non-mammalian species through thyroid modality. The amphibian metamorphosis assay is the most frequently available test. Attempts have been made to modify this protocol in order to make it more fit for purpose and overcome potential limitations. In light of these developments, EFSA, with the support of the Working Group on Endocrine Disruptors, under the auspices of a self-task mandate here endeavours to clarify the pros and cons of newly proposed amphibian protocols when compared with the standard guideline tests. Moreover, recommendations to facilitate the interpretation of findings in relation to changes in thyroid histopathology have been included. https://doi.org/10.2903/j.efsa.2025.9815

Maternal Exposure to 2,4-Di-tert-butylphenol During Pregnancy in a Mouse Model Leads to Abnormal Development of the Urinary System in Offspring,
Jiang, Y. Y., Ye, N. L., Yu, M. H., Ju, H. X., Wang, C. Y., Wang, H. M., Liu, J. J., Shen, Q. and Xu, H., *Toxics*, Nov 18 2025, Vol. 13, no. 11.

The occurrence of congenital anomalies of the kidney and urinary tract (CAKUT) is influenced by intrauterine environmental factors, and maternal exposure to endocrine-disrupting chemicals (EDCs) during pregnancy may affect the kidney development of offspring. 2,4-Di-tert-butylphenol (2,4-DTBP) is a high-production volume chemical classified as an EDC, which has been detected in humans and has been found to increase mortality and malformation rates in zebrafish embryos. Its effects on mammalian development are still unknown. In this study, a maternal mouse model exposed to 2,4-DTBP throughout pregnancy was established by gavage. The overall conditions of the maternal mice and their offspring were observed, and the concentrations of 2,4-DTBP in maternal serum and offspring tissues were measured using liquid chromatography-tandem mass spectrometry. Exposure to 2,4-DTBP of 75 mu g/g<middle dot>day during pregnancy markedly reduced the early pregnancy rate in mice to 41.75% (95% CI: 33.53-49.97%; n = 139), compared to 82.29% (95% CI: 74.18-90.39%; n = 85) in the controls (p < 0.0001), with a relative risk (RR) of 0.51 (95% CI: 0.41-0.63). 2,4-DTBP could accumulate in maternal mice and be transferred to embryos and internal organs of the offspring, and is associated with the elevated risk of CAKUT in the offspring, primarily manifesting as hydronephrosis/ureteral dilation. The CAKUT rate of DTBP-75 group is 33.59% (95% CI: 17.62-49.56%; N = 9, n = 56), compared to 11.85% (95% CI: 2.43-21.28%; N = 9, n = 67) in the controls (p = 0.02), RR = 2.53 (95% CI: 1.18-5.42). These findings enhance the understanding of the health risks posed by 2,4-DTBP and provide a theoretical basis for environmental monitoring in public health. https://doi.org/10.3390/toxics13110991

Co-exposure to low levels of DEHP, procymidone, Cd2+, Pb2+, and 1-nitropyrene may damage mouse ovary and uterus via Hippo pathway and circPVT1,
Li, Y. S., Nie, H., He, S. Y., Zhang, J. X., Fu, H. and Zhu, Y. F., *Toxicology Letters*, Dec 2025, Vol. 414.

High doses of Di-(2-ethylhexyl) phthalate (DEHP), procymidone (PCM), Cd2+, Pb2+, and 1-nitropyrene (1-NP) induce reproductive toxicity in female experimental animals. However, evidence regarding female reproductive toxicity at low levels of combined exposure (co-exposure) to these substances is lacking. In this study, these environmental chemicals, which met or minimally

exceeded the relevant standards, were administered simultaneously to 4-week-old female mice. After 21 days of exposure, the mice were kept feeding for 1 week and then sacrificed. Subsequently, their blood, ovaries, and uteri were taken. Co-exposure to concentrations >= 1/3 of the maximum allowable concentration (MAC) for each of these chemicals, as per relevant standards, was revealed to impair ovarian and uterine development in mice. This exposure activated the Hippo pathway, resulting in a decrease in ER alpha and circPVT1, and an elevation of miR-149. Co-exposure to these compounds in levels marginally lower than the MACs of each chemical also elevated cleaved CASPASE-3 levels. These changes showed a dose-response relationship. Joint exposure to these substances at values >= 1/3 of each average concentration in the blood could elicit similar biological effects in the ovaries and uteri cultured in vitro. Therefore, this study hypothesized that co-exposure to low levels of these environmental chemicals results in ovarian and uterine impairment in mice and that this damage may be linked to the activation of the Hippo pathway, downregulation of ER alpha and circPVT1, and upregulation of miR-149. https://doi.org/10.1016/j.toxlet.2025.111770

Sex- and Lineage-Dependent Transgenerational Effects of Vinclozolin and Flutamide on Rat Development and Behavior,
Morales-Grahl, E., Thompson, L. M., Krishnan, K., Crews, D. and Gore, A. C., *Journal of the Endocrine Society*, Jan 2026, Vol. 10, no. 1.

Vinclozolin (VIN) is an agricultural fungicide that acts as an endocrine-disrupting chemical (EDC), primarily through its anti-androgenic actions. Developmental exposure to VIN is linked with reproductive and neurodevelopmental alterations; furthermore, VIN was the first EDC identified as causing heritable epigenetic transmission across generations. The present study provides a more detailed and comprehensive look into the developmental and transgenerational behavioral effects of VIN exposure in rats, with the experiment designed to investigate the influence of sex differences and parental lineage (maternal, paternal). Specifically, dams were exposed to either the vehicle (DMSO; negative control), VIN (100 mg/kg), or flutamide (FLUT; 1 mg/kg), the latter an anti-androgenic compound used as a positive control for the anti-androgenic effects of VIN. Developmental measures, anxiety, and social tests were conducted on males and females from the F1 (direct prenatal exposure) and F3 (ancestral exposure through epigenetic inheritance) generations. Generally, effects were sexually dimorphic, lineage-specific, and differed between FLUT and VIN, pointing to different mechanisms of the chemicals. More behavioral effects of VIN emerged at the F3 generation's paternal lineage compared to the F1 generation. Overall, this study provides more detailed insight into the transgenerational effects of a high dose of VIN exposure and suggests future inquiry into the mechanisms of action of the EDC, specifically as it pertains to its differences from FLUT and its differing effects on lineage, sex, and generation.
https://doi.org/10.1210/jendso/bvaf175

A review of the effects of benzo(α)pyrene on amphibians,
Valverde, B. S. D., Carvalho, C. D. and De Oliveira, C., *Ecotoxicology*, Dec 5 2025, Vol. 35, no. 1.

In this overview, we address both in vitro and in vivo studies involving amphibians and the environmental contaminant benzo(alpha)pyrene (B alpha P). We indentified 66 papers published between 1939 and 2025, encompassing 23 species - 16 from the order Anura and 7 from the order Caudata, with no studies on Gymnophiona. Across these studies, regardless of taxonomic group, amphibians exhibited rapid absorption and metabolism of B alpha P (within 24 h), leading to the formation of secondary metabolites such as diols, which act as precursors of carcinogenic compounds capable of inducing DNA strand breaks. Following these initial processes, anatomical, physiological, and ultrastructural changes begin to occur. The progression of effects typically starts with genetic damage (e.g. adducts, breaks, and mutations) which alter the expression of genes

related to metabolism and cellular structures. Subsequent histopathological effects include pigmentary changes, tissue disorganization, and leukocyte infiltration, which, if persd leukocyte infiltration, which, if persistent, can lead to pathologies, malformations, and tumors. These effects may result in permanent damage that can be transmitted to subsequent generations. In addition to examining the biological effects of B alpha P, this overview also summarizes key methodological aspects of the reviewed papers, including exposure routes, concentration, dilution and duration of exposure. This work aims to serve as a valuable reference for future investigations, while also identifying knowledge gaps and guiding new experiments and research efforts.
https://doi.org/10.1007/s10646-025-02985-7

Aluminum exposure induces ferroptosis in spermatogenic cells of mice through iron overload and lipid peroxidation,
Wei, G. J., Peng, H. X., Hu, H. F., Lan, H., Feng, Y., Luo, S. H., Huang, Y. X., Yuan, H. X. and Chen, W. C., *Free Radical Biology and Medicine*, Dec 16 2025, Vol. 241, p. 789-806.

Aluminum (Al) is a pervasive environmental contaminant with detrimental biological effects. Although Al exposure induces oxidative stress and toxicity in spermatogenic cells, leading to impaired male reproductive function, the underlying molecular mechanisms remain incompletely elucidated. In this study, we systematically evaluated the toxic effects of Al on spermatogenic cells using both in vivo and in vitro models. Transcriptomic profiling of GC-2spd cells revealed Al-induced differential gene expression related to oxidative stress response, iron homeostasis, and lipid metabolism regulation. These alterations were notably enriched in the ferroptosis and HIF-1 signaling pathways. Subsequent in vivo analyses demonstrated that Al exposure increased iron levels and oxidative stress while reducing ATP content in mouse testes, resulting in testicular damage, decreased sperm quality, and lowered serum sex hormone levels, all of which contribute to reproductive dysfunction. Further investigations confirmed that Al disrupts redox and iron homeostasis, promoting lipid peroxidation and ferroptosis in both mouse testes and GC-2spd cells. Importantly, administration of the ferroptosis inhibitor Ferrostatin-1 (Fer-1) effectively restored homeostasis, thereby alleviating Al-induced ferroptosis and spermatogenic cell toxicity. In conclusion, this study demonstrates that Al disrupts iron and redox balance, leading to iron accumulation and lipid peroxidation in spermatogenic cells, which triggers ferroptosis and ultimately causes male reproductive impairment. These findings identify ferroptosis as a novel therapeutic target for mitigating aluminum-related reproductive risks and provide a scientific basis for public health interventions in occupational and environmental settings grounded in this newly characterized cell death mechanism. https://doi.org/10.1016/j.freeradbiomed.2025.09.043

Study on Hepatotoxicity of Benzophenone-3 at Environmental Concentration in Postpartum Mice,
Zhai, H. F., Tian, Y. N., Sheng, Y. X., Pu, Y. J., Gao, Y. R., Chen, J. Y., Liu, J. D., Ma, J., Xu, H. M., Yang, P. B. and Li, H. M., *Toxics*, Nov 22 2025, Vol. 13, no. 12.

Benzophenone-3 (BP-3), a widely used ultraviolet absorber in various scenarios, exhibits estrogenic toxicity at environmental concentrations-as demonstrated in our prior work. Given the importance of hepatic metabolism and the limitations of previous hepatotoxicity research (high-dose models, lack of mammalian data, etc.), we evaluated BP-3's hepatic effects on postpartum mice at environmentally relevant levels. Postpartum mice were exposed to BP-3 via drinking water from postpartum day 1 (PPD1) to PPD35. Groups solvent control (0.001% DMSO), 10-1000 nM BP-3, and diethylstilbestrol (DES) were established. Basic growth performance, histopathological changes, and a range of molecular indicators were assessed. The results showed that BP-3 exposure induced dose-dependent increases in liver weight, histopathological alterations (sinusoidal dilation, hepatocyte edema, and necrosis), and significant upregulation of oxidative stress markers (Ros, Mda),

chemokines (Ccl27a/b), and inflammatory factors (Tnf-α, Il-6, Nf-κb) at the mRNA level (all p < 0.05). Conversely, levels of antioxidant enzymes (Cat, Sod1/2) and anti-inflammatory factor Ho-1 were markedly decreased (p < 0.05). A clear dose-effect relationship was confirmed using the Integrated Biomarker Response (IBR) framework. This pioneering study establishes the hepatotoxicity of environmentally relevant BP-3 levels in mammals and offers methodological insights for endocrine disruptor assessment. https://doi.org/10.3390/toxics13121014

A meta-analysis-based adverse outcome pathway for the reproductive toxicity induced by perand poly-fluoroalkyl substances in animals,
Zhu, Y., Zhao, C., Guo, H., Shi, Q. T., Dong, R. J., Wang, Q. Q., Wu, Y. and Zhang, H., *Toxicology*, Feb 2026, Vol. 520.

Per- and poly-fluoroalkyl substances (PFAS) were highly toxic to reproductive systems due to the widespread environmental distribution and persistence. However, the underlying mechanisms were not well understood. This study systematically evaluated the association between existing adverse outcome pathways (AOPs) and PFAS-induced reproductive toxicity using the AOP conceptual framework. A meta-analysis of 28 studies quantified the effect sizes, providing a comprehensive assessment of PFAS-induced reproductive toxicity in animals. Within the AOP framework, the molecular initiating event (MIE) was increased reactive oxygen species (ROS), which triggered several key events (KEs) at different levels. At the cellular level, the KEs included oxidative stress, mitochondrial dysfunction, DNA damage, endoplasmic reticulum stress, reduced steroidogenic protein expression, decreased thyroid hormone synthesis, epigenetic modification process, lipid metabolism disorders, decreased androgen and estrogen receptors. These KEs led to decreased testosterone and elevated estrogen levels, alongside disruptions in spermatogenesis, oocyte maturation, and ovulation. Consequently, this resulted in lower sperm count, impaired sperm quality, and decline in oocyte quantity. Meta-analysis results showed that PFAS exposure significantly decreased juvenile survival rates (Standardized Mean Difference (SMD): -3.10, 95 % Confidence Interval (CI): -4.01, -2.18), reduced male testosterone (SMD: -4.17, 95 % CI: -6.00, -2.33) and female estradiol levels (SMD: - 1.98, 95 % CI: -3.15, -0.81) in animals. Our findings systematically summarized the reproductive toxicity mechanisms of PFAS and alternatives, providing scientific basis for assessing the environmental impact.
https://doi.org/10.1016/j.tox.2025.154352