Bulletin de veille Perturbateurs Endocriniens N°35 – Mars/Avril 2026

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

La validation des informations fournies (exactitude, fiabilité, pertinence par rapport aux principes de prévention, etc.) est du ressort des auteurs des articles signalés dans la veille. Les informations ne sont pas le reflet de la position de l'INRS.

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

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Exposition professionnelle

Pesticides associated with incident diabetes among licensed private pesticide applicators in the Agricultural Health Study cohort (1993-2021).

Parks CG, Xiao Q, Wilkerson J, Hofmann JN, Beane Freeman LE, Sandler DP. *Environ Int*. 2026 Feb;208:110082.

BACKGROUND: Growing evidence suggests pesticides may increase risk of type 2 diabetes, but data are limited on many specific chemicals. METHODS: In 29,527 private pesticide applicators in the Agricultural Health Study cohort (enrolled 1993-1997 in Iowa and North Carolina), 3,847 incident diabetes cases were identified by self-report during follow-up surveys in 1999-2003, 2005-2010, 2013-

2015, and 2019-2021. We examined 50 pesticides reported at enrollment, updated in 1999-2003 or 2005-2010, prior to diabetes diagnosis or end of follow-up, using log-binomial regression to calculate relative risks (RR) and 95% confidence intervals (CI) for ever-use and intensity-weighted lifetime days (IWLD) use (tertiles, T1-3), adjusting for covariates and correlated pesticides. FINDINGS: Greater diabetes risk was associated with 7 organochlorine insecticides: ever-use of DDT, aldrin, dieldrin, chlordane, heptachlor, and toxaphene (RRs 1.08-1.31), without monotonic exposure-response trends, and lower IWLD of lindane use ((T1)RR=1.32; 95%CI 1.12-1.57). Risk was associated with 5 organophosphate or carbamate insecticides: ever-use of diazinon and carbofuran, and exposure-response trends for malathion ((T3)RR=1.13;95%CI 1.02-1.25, p-trend=0.025), phorate ((T3)RR=1.22;95%CI 1.08-1.39, p-trend=0.001), and carbaryl ((T3)RR=1.26;95%CI 1.11-1.43, p-trend=0.005). Risk was associated with 2 phenoxy herbicides, 2,4,5-T (ever-use RR=1.25;95%CI 1.14-1.37) and 2,4,5-TP ((T1)RR=1.35;95%CI 1.04-1.76), and 3 other herbicides [butylate ((T3)RR=1.26;95%CI 1.10-1.44, p-trend<0.001), metribuzin ((T3)RR=1.16;95%CI 1.16-1.32, p-trend=0.022), chlorimuron ethyl ((T3)RR=1.16;95%CI 1.02-1.31, p-trend=0.033)], and the fumigant carbon tetrachloride/disulfide (RR=1.16;95%CI 1.02-1.33). Associations were not confounded by BMI and weight gain. CONCLUSIONS: These results show greater diabetes risk associated with use of persistent organochlorine insecticides and banned phenoxy herbicides. Novel findings for widely used insecticides and other pesticides warrant further investigation.

Lien vers l'article

Hormonal changes in professional printers exposed to phthalates suggesting potential disturbances of the hypothalamic-pituitary-gonadal axis.

Nita TM, Wrobel SA, Vernez D, Koch HM, Wild P, Zufferey F, et al. *Environ Res*. 2026 Feb 15;291:123477.

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.

Lien vers l'article

Occupational Exposure to Resorcinol and Thyroid-Disrupting Effects: Protocol for an Exploratory Field Study in French Hairdressers.

Radauceanu A, Cambrai-Erb A, Adet B, Nioule MI, Denis F, Pons R. *JMIR Res Protoc*. 2026 Mar 31;15:e65833.

BACKGROUND: All around the world, the hairdressing sector constitutes a major occupational group, including about 90% women, most of whom are of reproductive age. Hairdressers are continuously exposed to numerous chemicals used in hair products, including endocrine-disrupting compounds such as resorcinol, parabens, phthalates, and UV filters. Few biomonitoring studies have explored occupational exposure to endocrine disruptors in hairdressers, and no data were found on their impact on the thyroid hormone system. Resorcinol is an oxidative hair dye with thyroid-disrupting properties that decrease thyroid hormone synthesis and could alter neurodevelopmental functions during fetal and perinatal stages in case of maternal exposure. OBJECTIVE: This study aims to assess the occupational exposure to resorcinol in French hairdressers and analyze the relationship with biological thyroid parameters, taking into account the occupational exposure to other potential thyroid disruptors (parabens and UV filters like benzophenone and cinnamates). METHODS: An exposed-unexposed cross-sectional study is proposed involving female hairdressers aged 18 to 45 years (working in hair salons) compared to occupationally unexposed controls (employed in office activities), who are recruited within 14 French occupational health centers. The hairdressers are followed during a 5-day working week to assess exposure data at both the individual level and the salon level. Urinary samples for the measurement of thyroid disruptors (resorcinol, parabens, metabolites of ethylhexyl methoxycinnamate, and benzophenone-3) are collected at 6 time points (before the day 1 shift, before and after the day 3 and day 4 shifts, and before the day 5 shift). Daily work tasks and use of hair products are self-reported within the workplace, and a complete inventory of hair products within the salon is carried out. Thyroid disruption effects are assessed by measuring blood thyroid parameters: triiodothyronine, thyroxine, thyroid-stimulating hormone, thyroglobulin, thyroperoxidase, and thyroglobulin antibodies. To assess nonoccupational exposure to thyroid disruptors and other confounding factors, information on sociodemographic data, place of residence, food and tobacco consumption, personal use of care products, professional career, and medical history is collected through questionnaires. Regarding statistical analysis, urinary samples from hairdressers and controls will be compared, and adjusted multivariable models will be used to analyze health outcomes. RESULTS: The study duration extends from 2022 to 2027. As of December 2025, 9 occupational health centers have enrolled 66 hairdressers (employed in 54 hair salons) and 30 occupationally unexposed participants. CONCLUSIONS: The results will represent the first data on occupational exposure to resorcinol in France and its relationship with thyroid hormones in hairdressers. Following a multidisciplinary approach that includes biomonitoring, epidemiology, and exposure data collection at both the hairdressers and salon levels, this study enables an in-depth assessment of exposure to the thyroid disruptors in the workplace. Together with the inventory of hair products, these results may enhance the tools for chemical risk assessment and prevention in hair salons.

Lien vers l'article

Occupational exposure to endocrine-disrupting chemicals and colorectal cancer risk - An analysis of four participating cohorts of the Canadian Partnership for Tomorrow's Health study.

Pelland-St-Pierre L, Siemiatycki J, Dummer T, King WD, Koushik A, Lavoué J, et al. *Environ Res*. 2026 Mar 18;299:124299.

INTRODUCTION: Endocrine-disrupting chemicals (EDCs) may influence cancer risk by interfering with sex hormone balance. Yet, the role of EDCs in colorectal cancer remains underexplored. EDC exposure is common in the environment, but levels are much higher in certain workplaces. This study assessed the association between occupational exposure to selected EDCs and colorectal cancer risk. METHODS: A case-cohort study was nested within four regional cohorts of the Canadian Partnership for Tomorrow's Health study. Cases included 1083 incident colorectal cancer cases, and a subcohort of 4788 participants was selected at baseline. Occupational exposure to 17 EDCs in participants' longest-held job was estimated using CANJEM, a job exposure matrix, which provided the probability of exposure for each EDC-job combination. Participants were categorized into unexposed (probability = 0), possibly exposed (0<probability<25%) or exposed (probability≥25%) for each EDC. Exposure was conceptualized in three ways: any exposure, grouped by mode of action (estrogenic, antiestrogenic, and antiandrogenic), and individual EDCs. Odds ratios (OR) and 95% confidence intervals (95%CI) were estimated between EDC exposure and colorectal cancer in each regional cohort and pooled using fixed-effect models. RESULTS: Compared to unexposed participants, participants exposed to antiestrogenic EDCs had an elevated colorectal cancer risk (OR = 1.31, 95%CI: 1.01-1.70). Risk was increased for possible exposure to arsenic (OR = 1.67, 95%CI: 1.27-2.21) and polychlorinated biphenyls (OR = 3.34, 95%CI: 2.20-5.07). Participants possibly exposed to cadmium (OR = 0.78, 95%CI: 0.63-0.96) had a lower colorectal cancer risk. CONCLUSION: We observed some associations between occupational EDC exposure and colorectal cancer risk. Further investigation of these relationships is warranted.

Lien vers l'article

Indirect exposure to organophosphate pesticides and its possible growth disorders in children of farmers in Northwest Mexico.

Ochoa-Ruiz E, Moreno-García AI, Licea-Espinoza DA, Pineda-García G, Carranza-Ambriz KP, Soto-Rodriguez KK, et al. *Int Arch Occup Environ Health*. 2026 Jan 27;99(2):11.

***Purpose** : This study investigated the correlation between growth disorders and indirect pesticide exposure in children of farmers.*
***Methods** : A cross-sectional study was conducted with 134 children of farmers occupationally exposed to organophosphate pesticides in the ejido Venustiano Carranza, an agricultural community in San Quintín, Baja California, Mexico. These children were compared with a control group of 56 unexposed children. Anthropometric measurements and biochemical analyses were performed in both groups to evaluate renal, hepatic, and nutritional profiles. Hormonal profiles were quantified using ELISA techniques. Cholinesterases are quantified using known colorimetric methods. Food security was also analyzed through a dietary diversity study, focusing on households.*
Results Indirectly exposed group showed a higher prevalence of stunting (18% vs. 16.4%) than controls. Food safety was adequate in both groups (X2=1.88, p=0.597). The indirectly exposure children showed significantly higher calcium levels (9.99±0.63 mg/dL) and significant increases in liver enzymes AST and GGT (p<0.001). ALP was 1.5 times lower than in unexposed children (p<0.001), showing a strong association with exposure time (p=0.009). The indirectly exposed group showed lower GH and IGF-1 levels; 2.55 and 1.28 times lower than in controls, respectively. Children with indirect exposure showed a significant reduction in AChE (7211±1917 vs. 8368±213 U/L, p<0.001) and an even greater decrease in BChE (6426±1664 vs. 8025±1462 U/L, p<0.001).
***Conclusion** : This work demonstrates an association between environmental exposure to organophosphate pesticides and children's growth and provides crucial insights for future research and policymaking.*

Lien vers l'article

Breast cancer-related occupational exposures facing immigrant women.

Knox KE, Ohayon JL, Carrera E, Rudel RA, Morello-Frosch R. *J Expo Sci Environ Epidemiol*. 2026 Mar;36(2):355-60.

BACKGROUND: Immigrants comprise roughly 14% of the U.S. population, and studies indicate that breast cancer increases among some immigrant groups after relocating to the U.S. OBJECTIVE: We characterized exposures to breast cancer-relevant chemicals in jobs commonly occupied by U.S. immigrant women, aged 18-65. METHODS: We analyzed data from the American Community Survey Public Use Microdata Sample to profile which occupations are most prevalent for immigrant women and integrated these results with data on occupational chemical exposures from the Women's Occupations and Risk from Chemicals tool, which identifies occupations with probable and possible chemical exposures of relevance for breast cancer. RESULTS: Immigrant women most commonly work as house cleaners, nurses, cashiers, janitors, and care aides, and comprise 71% of manicurists. We prioritize the occupations house cleaners and nurses for their combination of high potential exposures and the large number of immigrant women employed in these occupations. Chemicals of interest are those found in fragrances, and cleaning and maintenance products, including phthalates, antimicrobials, and alkylphenols. Many of these compounds are mammary gland carcinogens and developmental toxicants, and/or endocrine disruptors. IMPACT: There are few studies of breast cancer-relevant chemical exposures for most occupations, including those heavily represented by immigrant women. By identifying jobs that employ large numbers of immigrant women and are associated with a high likelihood of exposure to potential breast carcinogens, we inform future research on breast cancer-relevant exposures and opportunities for preventative exposure reduction. We also show that immigrant women with lower levels of education and English fluency work in occupations with more potential for harmful chemical exposures.

Lien vers l'article

Prenatal occupational exposure to endocrine-disrupting chemicals during pregnancy and adult male reproductive hormones.

Blanc-Petitjean P, Rahban R, Dananché B, Senn A, Zufferey F, Stettler E, et al. *Reprod Biomed Online*. 2026 Mar;52(3):105236.

RESEARCH QUESTION: Does maternal occupational exposure to endocrine-disrupting chemicals (EDC) during pregnancy affect reproductive hormone concentrations in adult sons? DESIGN: Data from a cross-sectional study of 2326 Swiss conscripts collected between 2005 and 2017 were analysed. On inclusion, the conscripts' mothers completed a detailed questionnaire about their pregnancy. A job-exposure matrix was used to assess exposure to 10 categories of potential EDC. Reproductive hormones - FSH, LH, total and free testosterone, oestradiol and sex hormone-binding globulin (SHBG) - were determined in serum samples from all conscripts whose mothers were exposed to EDC during pregnancy (n = 138) and a random sample of non-exposed conscripts (n = 276). Multiple linear regression analyses were adjusted for potential confounders. RESULTS: Prenatal exposure to phthalates or alkyl phenolic compounds was significantly associated with higher FSH concentrations (aβ = 0.26, 95% CI 0.03-0.49, and aβ = 0.22, 95% CI 0.02-0.42, respectively) and prenatal exposure to pesticides was significantly associated with higher SHBG concentrations (aβ = 0.22, 95% CI 0.05-0.38). No statistically significant associations were found between other EDC categories and reproductive hormones. CONCLUSIONS: Maternal occupational exposure to certain types of EDC during pregnancy

was associated with the concentrations of reproductive hormones in adult sons. These findings require replication in larger, prospective population studies.

Lien vers l'article

Prenatal exposure to pesticides and the risk of male genital malformations: A scoping review, Ariza, M., Lakehal, N., Fiani, M., Chardon, K. and Haraux, E., *Reproductive Toxicology*, Aug 2026, Vol. 143.

Introduction: Hypospadias and undescended testis (UDT) are common genital malformations with multifactorial origins. Endocrine-disrupting chemicals, including pesticides, are suspected contributors, but prior reviews are outdated, and none has mapped evidence for both conditions together. Objective: To map evidence on the association between prenatal pesticide exposure and hypospadias/UDT, with particular attention to underexplored exposures such as pyrethroids and household pesticides, and to identify research gaps. Method: Following PRISMA-ScR guidance, we searched PubMed, Web of Science, Cochrane, and Embase from 2003 to 2024. Eligible items were original human studies and reviews. Study selection and data extraction were performed by two reviewers. Results: We included 117 articles (62 case-control studies, 7 population-based/cohort/epidemiological studies, 4 meta-analyses, and 44 reviews). Evidence from primary studies was heterogeneous across designs, but several signals recurred: increased risks associated with maternal occupational or residential exposure in agricultural settings; positive associations when exposure was assessed using bioaccumulative matrices (placenta, breast milk, meconium); and limited or null findings with single time-point blood/urine measures. Data on household insecticides use remain scarce, particularly for pyrethroid insecticides. Few studies examined gene-environment interactions. Conclusion: This scoping review highlights suggestive but inconsistent evidence that prenatal pesticide exposure contributes to hypospadias/UDT, with organochlorines (e.g., DDT/DDE, atrazine) most frequently implicated. Key gaps include pyrethroid exposure, prospective designs with improved exposure assessment, and stronger links between human epidemiological findings and existing mechanistic evidence. While causal inference is limited in a scoping review framework, the overall body of evidence supports adopting a precautionary approach to minimizing pesticide exposure during pregnancy. https://doi.org/10.1016/j.reprotox.2026.109238

Hidden risks associated with occupational pesticide exposure in women with breast cancer: High frequency of the Luminal B molecular subtype and occurrence of poor prognostic features, Cazagranda, I. C., De Almeida, R. F., Smaniotto, L. L., Berny, M. P. D., Coradi, C., Rech, D., Panis, C. and Silveira, G. F., *Plos One*, Feb 5 2026, Vol. 21, no. 2.

Human pesticide exposure is a common event in countries with strength conventional agriculture, such as Brazil. Despite evidence on the negative impact of pesticides on human health, the country stands out among the top three pesticide consumers globally. The implications of this scenario on rural workers health, particularly women, is completely neglected, resulting in chronic illness such as breast cancer. Objective: In this study, we analyzed the impact of occupational/household chronic exposure to pesticides on the clinicopathological profile of breast cancer in rural women from Paran & aacute; southwest, a predominantly rural landscape with large pesticide uses. Methods: A total of 349 women were included in the study. After a structured interview, women were categorized as exposed (n = 208) or unexposed (n = 141) to pesticides. Clinicopathological data were collected from medical records. Descriptive and inferential statistical methods were used to characterize and compare the sample. The Chi-square test and Fisher's exact test were used to evaluate differences between the molecular subtypes and clinicopathological variables of patients. Results: Exposed

patients had a prevalence of the Luminal B subtype (32.83%), while unexposed patients had a prevalence of the Luminal A molecular subtype (37.78%, p <= 0.05). Exposed patients also had higher disease recurrence (10.19%), chemoresistance (21.26%), than unexposed patients (p <= 0.05). Breast cancer patients exposed to pesticides were also more likely to have distant metastases (1.4 times) and lymph node invasion (1.3 times) compared to patients not exposed. Conclusions: These findings indicate that pesticide exposure favors the occurrence of more aggressive breast cancer. https://doi.org/10.1371/journal.pone.0339471

Effect of occupation on assisted reproduction outcomes in an oocyte donor model,
Lee, J. C., Thornburgh, S., Nagy, Z. P., Shapiro, D. B., Hipp, H. S. and Gaskins, A. J., *Archives of Environmental & Occupational Health*, Apr 21 2026, Vol. 81, no. 3-4, p. 95-104.

Previous studies have linked workplace conditions, including chemical and physical exposures, and reproductive health outcomes in women. Our study included 603 oocyte donors who underwent 967 controlled ovarian hyperstimulation (COH) cycles for planned oocyte vitrification between 2008 and 2020. Cohorts of oocytes were then thawed and fertilized with resultant embryos utilized by intended parents. In our cohort of young, healthy oocyte donors, those employed in "healthcare practitioners and technical" occupations and in "office and administrative support" roles had lower ovarian reserve testing by antral follicle count and fewer mature oocytes retrieved COH when compared to the reference group. In vitro fertilization and embryo transfer outcomes, including live birth, for oocyte recipients were not statistically different between occupation groups when compared to the reference group. Future research is needed to clarify specific occupational exposures that may be driving these observed differences. https://doi.org/10.1080/19338244.2026.2640098

Linking Pesticide Exposure to Gestational Diabetes: Current Knowledge and Future Directions,
Pagkaki, C., Tsikouras, P. and Halvatsiotis, P., *Physiologia*, Jan 5 2026, Vol. 6, no. 1.

Background: Gestational diabetes mellitus (GDM) is a frequent pregnancy pathology with poor maternal and fetal outcomes and risk of type 2 diabetes in later life. Despite known risk factors, such as obesity, age, and familial history, new data suggest that environmental exposure to agents, such as pesticides, can play a role in the etiogenesis of GDM. Objective: The epidemiologic, experimental, and mechanistic evidence between pesticide exposure and GDM risk is summarized here, and we concentrate on recent research (2000-2025). Methods: We conducted a literature search in PubMed, Embase, and the Cochrane Library for studies published from January 2000 to December 2025 using combinations of the terms "fertilizers", "herbicides", and "pesticides" with "diabetes mellitus" and "gestational diabetes". After deduplication, 12 unique studies met inclusion criteria for qualitative synthesis (GDM endpoint or pregnancy glycemia with pesticide exposure). Results: Occupational and agricultural exposure to pesticides during first pregnancy was determined to be associated with a significantly increased risk of GDM through various epidemiologic studies. New studies have implicated new classes of pesticides, including pyrethroids and neonicotinoids, with higher GDM risk with first-trimester exposure. Experimental studies suggest that pesticides provide potential endocrine-disrupting chemicals that can induce insulin resistance through disruption of hormonal signaling, oxidative stress, inflammation, beta-cell toxicity, and epigenetic modifications. However, significant limitations exist. Most of the evidence is observational, measurement of exposure is often indirect, and confounding factors are difficult to exclude. Notably, low dietary and residential exposure is not well studied, and dose-response relationships are undefined. Conclusions: New data indicate that pesticide exposure during early pregnancy and occupational exposure may increase the risk of GDM. Prospective cohort studies using biomonitoring, chemical mixture exposure, and geographic variation in pesticide exposure should be the focus of future research. Due to potential public health implications, preventive strategies to ensure the quality of nutrition and to reduce

maternal exposure to pesticides during pregnancy are rational. https://doi.org/10.3390/physiologia6010004

Perfluorooctane sulfonate (PFOS) in follicular fluid and human granulosa cell dysfunction: a physiologically based toxicokinetic model translation of long-term low-level in vitro exposure data, Tomanic, T., Nenadov, D. S., Pletikosic, S. R., Stanic, B., Obradovic, D., Lazovic, S. and Andric, N., *Human Reproduction Open*, 2026 2026, Vol. 2026, no. 2.

STUDY QUESTION Are bioactive human-equivalent doses (HEDs) of perfluorooctane sulfonate (PFOS), derived from long-term low-level in vitro exposure of human granulosa cells comparable to HEDs inferred from follicular fluid PFOS concentrations in women undergoing ART and in occupationally exposed women? SUMMARY ANSWER The bioactive HEDs overlapped with and, in some cases, were lower than the median HEDs inferred from follicular fluid PFOS concentrations. WHAT IS KNOWN ALREADY PFOS exposure is a growing public health concern, with evidence suggesting adverse female reproductive effects. However, the relevance of current human exposure levels to granulosa cell function remains unclear. STUDY DESIGN, SIZE, DURATION Four independent vials of human granulosa cells (HGrC1 cells) were thawed and expanded into separate flasks (biological replicates). Cells were allocated to four experimental groups and exposed to PFOS (0.01, 0.1, or 1 µM) or vehicle control (0.05% DMSO) for up to 12 weeks, with re-dosing at each passage. Different apical endpoints, along with transcriptomic changes, were evaluated at designated time points. Clinical relevance of PFOS risk to human granulosa cells was assessed by integrating experimental data with physiologically based toxicokinetic (PBTK) modeling. PARTICIPANTS/MATERIALS, SETTING, METHODS Viability of HGrC1 cells was assessed using the Alamar Blue assay. Estradiol and progesterone secretion were quantified by enzyme-linked immunosorbent assay. Flow cytometry was used to determine the proportions of live, apoptotic and necrotic cells, as well as cell cycle distribution. Global mRNA expression was assessed by DNA nanoball sequencing technology (DNBSEQ), whereas pathway-level molecular functions were derived using bioinformatic tools. Benchmark concentrations (BMCs) were calculated from key endpoints with concentration-dependent responses and used to estimate HEDs via PBTK modeling. These HEDs were compared with HEDs inferred from follicular fluid PFOS levels reported in the literature to derive bioactivity exposure ratios (BERs) and assess relevance to human exposure. MAIN RESULTS AND THE ROLE OF CHANCE In HGrC1 cells, long-term PFOS exposure altered steroidogenesis, apoptosis/necrosis, cell cycle distribution ($P < 0.05$), and gene expression (at least 2-fold change, Q-value <= 0.05). Median transcriptomic HEDs were 18.1 (95% CI: 1.1-35.1) and 17.5 ng/kg bw/day (95% CI: 8-27.1) for 6- and 12-week exposures, respectively, with corresponding 5th percentile HEDs of 3.7 ng/kg bw/day (95% CI: 0.4-9.3) and 1.4 ng/kg bw/day (95% CI: 0.5-3.5). Pathway-level HEDs ranged from 2.8 to 24.1 ng/kg bw/day, with eicosanoid synthesis showing the greatest sensitivity. HEDs for apical endpoints ranged from 0.4 to 203 ng/kg bw/day, with the sub-G(1) cell cycle phase being most sensitive. HEDs derived from the 5th percentile transcriptomic data, eicosanoid metabolism, and the sub-G(1) phase yielded BERs below 1, indicating that PFOS levels measured in follicular fluid of ART patients may be sufficient to induce these biological effects. For occupational exposure, BERs derived from all endpoints were below 1. A subset of nine granulosa-cell genes, including CYP1B1 and TIPARP (aryl hydrocarbon receptor signaling), showed HEDs that were below the follicular-fluid-inferred HED, highlighting potential high-priority targets and candidate biomarkers. LARGE SCALE DATA Raw and processed RNA-sequencing data are deposited in NCBI Gene Expression Omnibus (GEO) under accession number GSE315651.LIMITATIONS, REASONS FOR CAUTION The estimated exposure values were based on predictions from a PBTK model rather than empirical human exposure data. Also, differences in protein concentrations in vitro and in vivo may affect free PFOS levels and bioactivity estimates. We addressed this with additional adjustments for PFOS-albumin binding. Finally, follicular fluid PFOS concentrations in occupational

settings were approximated from serum concentrations using blood-to-follicular fluid transfer efficiency (BFTE) values. WIDER IMPLICATIONS OF THE FINDINGS Our findings suggest that PFOS concentrations in follicular fluid from women undergoing ART and those who have been occupationally exposed may be sufficient to perturb granulosa cell mRNA expression and key pathways, including eicosanoid, interleukin, and GPCR signaling. The identified genes may serve as candidate biomarkers linking PFOS exposure to clinical outcomes in ART settings. Overall, this study provides a framework for interpreting PFOS reproductive toxicity and refining health-protective exposure thresholds. https://doi.org/10.1093/hropen/hoag029

The effect of occupational lead toxicity on testosterone secretion and the L-arginine nitric oxide pathway,
Tutkun, L., İritaş, S. B., Büyükşekerci, M., Türksoy, V. A., Özkan Vardar, D., Öztan, Ö., Deniz, S., Dedeoğlu, Z. and Tutkun, E., *Toxicology and Industrial Health*, 2026/04/10/ 2026, p. 7482337261441688.

Endocrine-disrupting chemicals (EDCs), including heavy metals such as lead (Pb), interfere with hormonal homeostasis, particularly in the hypothalamic-pituitary-gonadal (HPG) axis. Occupational lead exposure is linked to male reproductive dysfunction and cardiovascular risk via oxidative stress and endothelial impairment. This study investigated the effects of chronic lead exposure on testosterone levels and the L-arginine-nitric oxide (NO) pathway, a key regulator of endothelial function. This case-control study compared 120 male workers with occupational lead exposure (in battery manufacturing and foundries) to 120 unexposed controls. Blood lead levels (BLLs) were quantified via inductively coupled plasma mass spectrometry (ICP-MS), while testosterone (total/free) and methylated arginine metabolites; asymmetric dimethylarginine (ADMA), symmetric dimethylarginine (SDMA), arginine, and citrulline were analyzed using LC-MS/MS. Statistical analyses included t-tests and Pearson correlations to assess associations. Lead-exposed workers had significantly higher BLLs (31.76 ± 13.31 vs 1.72 ± 0.87 µg/dL), lower total testosterone (388.23 ± 71.78 vs 477.36 ± 104.21 ng/dL), and reduced arginine/ADMA ratios (432.48 ± 191.27 vs 544.33 ± 187.19), indicating endothelial dysfunction. Strong inverse correlations were observed between exposure duration, classified as 6 months to 1 year, 1 to 5 years, and >5 years, to evaluate its association with BLL, testosterone levels, and arginine metabolism markers. This study demonstrated that chronic occupational lead exposure significantly disrupted testosterone secretion and impaired the L-arginine-NO pathway, highlighting its dual threat to reproductive and cardiovascular health. The robust inverse correlations between BLL, testosterone, and arginine/ADMA ratios underscore the endocrine-disrupting and endothelial-damaging effects of lead. These findings support the routine biomonitoring of BLL, testosterone, and methylated arginine metabolites in high-risk occupations to enable early intervention and mitigate long-term health risks. https://doi.org/10.1177/07482337261441688

Occupational exposure to inhalational anesthetics and the risk of spontaneous abortion: a systematic review and meta-analysis,
Ying, T. and Yuanqing, W., *Frontiers in Public Health*, Apr 1 2026, Vol. 14.

Background: Healthcare professionals, particularly anesthesiologists, nurses, and dental staff, are routinely exposed to inhalational anesthetic agents such as nitrous oxide and halogenated gases. Although scavenging and ventilation systems have reduced ambient levels, concerns remain regarding reproductive risks associated with chronic exposure. Previous studies have yielded inconsistent results. A systematic review and meta-analysis of published observational studies was conducted to clarify the relationship, assessing reproductive outcomes among healthcare workers

who were exposed. Objective: This systematic review and meta-analysis aimed to clarify the association between occupational exposure to anesthetic gases and the risk of spontaneous abortion among healthcare workers. Methods: A systematic search was performed in PubMed, Scopus, and Web of Science up from inception until the end of July 2025. Observational studies assessing spontaneous abortion among female healthcare workers exposed to inhalational anesthetics were included. Two reviewers independently screened and extracted data and assessed study quality using the Newcastle-Ottawa Scale (NOS). Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using a random-effects model. Heterogeneity was evaluated using the I-2 statistic, and potential moderators were explored via subgroup and meta-regression analyses. Results: Seventeen studies were included. The pooled analysis showed 1.29-fold higher odds of spontaneous abortion among exposed workers compared with unexposed controls (OR = 1.29; 95% CI: 0.96-1.75; I-2 = 87%). Subgroup analyses indicated stronger associations in North American studies and among high-exposure occupations. Meta-regression analysis indicated that exposure duration is a significant predictor (p = 0.010), accounting for 73.6% of the heterogeneity. Sensitivity and Egger's tests revealed robust findings without evidence of publication bias. Conclusion: Occupational exposure to anesthetic gases may increase the risk of spontaneous abortion, particularly in those who are at high exposure, emphasizing the need for stringent exposure control and improved workplace safety standards. https://doi.org/10.3389/fpubh.2026.1766912

Epidémiologie

Associations of perfluoroalkyl and polyfluoroalkyl substances with markers of glycaemic control, insulin secretion and sensitivity, and diabetes risk: a systematic review and meta-analyses, Aldana, S. I., Yu, X., Yao, M. Z., Cohen, N., Markopoulou, E., Chowdhury, M., Midya, V., Eick, S. M., Trowbridge, J., Starling, A. P., Barupal, D., Walker, D. I., Chatzi, L., Setiawan, V. W., Walker, R. W., Colicino, E. and Valvi, D., *Eclinicalmedicine*, Feb 2026, Vol. 92.

Background Growing literature examines the impact of per-and polyfluoroalkyl substances (PFAS) on diabetes risk. We aimed to conduct a comprehensive systematic review and meta-analysis of epidemiological studies to characterize the associations of exposures to PFAS with markers of glycemic control, insulin resistance, pancreatic (3-cell function, and diabetes risk. Methods A systematic search of epidemiological articles published through July 21, 2025 was conducted by two researchers in PubMed/MEDLINE and Ovid/EMBASE following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Experimental studies were excluded from our review. Reported findings were extracted from published articles. Risk of bias was evaluated using the Navigation Guide. Random-effects meta-analyses stratified by study design estimated PFAS associations with gestational diabetes mellitus (GDM), type 2 diabetes (T2D), and continuous measures of Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), HOMA-(3, fasting insulin, fasting glucose, and hemoglobin A1c (HbA1c). This study was registered in PROSPERO (CRD42022369711). Findings Out of 738 records retrieved, we identified 129 eligible studies. Most studies focused on GDM (n = 25) and/ or T2D (n = 36), while three focused on type 1 diabetes (T1D). Participant numbers ranged from n = 40 to n = 1,331,541 in the systematic review and from n = 399 to n = 111,544 in the meta-analyses. We found consistent associations between 8 different PFAS and higher odds of GDM across prospective and other study designs, including PFOS [n = 8, OR (95%CI) per doubling PFOS increase: 1.13 (1.01, 1.26), I 2 = 0.0%] among other PFAS. We also found positive associations between several legacy PFAS such as PFOS with HOMA-IR [(n = 8), (3 (95%CI): 0.06 (0.01, 0.12), I 2 = 0.0%] and fasting insulin [n = 5, (3 (95% CI) in & micro;U/mL: 0.23 (0.06, 0.40), I 2 = 0.0%] in prospective studies, and HOMA-(3 in cross-sectional studies [(n = 6), (3 (95% CI): 5.93 (1.72, 10.2), I 2 = 67.0%], among other. Less consistent or null associations were with T2D, fasting glucose, and

HbA1c. The evidence was of low-moderate quality and limited strength. Most studies were categorized as low risk of bias for other criteria, except for study design (cross-sectional). Interpretation Evidence from observational studies supports PFAS associations with higher odds of GDM and increased markers of insulin resistance and secretion. PFAS associations with established T2D or T1D remain to be elucidated, as evidence is still limited and effect sizes for some continuous diabetes markers were small and should be interpreted with caution. Larger life-course prospective studies with greater representation of well-characterized cases and evaluating emerging PFAS and mixtures are needed to fully capture the potential PFAS impacts on diabetes. https://doi.org/10.1016/j.eclinm.2025.103747

Impact of antenatal exposure to a mixture of endocrine disruptors on attentional and executive functions in children,
Barrea, C., Dufour, P., Pirard, C., Charlier, C., Brévers, F., Parent, A. S. and Rousselle, L., *Journal of the Endocrine Society*, Apr 2026, Vol. 10, no. 4.

Context Numerous studies indicate negative associations between early life exposure to endocrine-disrupting chemicals and various aspects of neurodevelopment. However, few have focused on specific cognitive processes. Additionally, toxicants are often analyzed individually, without accounting for their combined effects. Objective This study aimed at investigating the impact of prenatal exposure to a mixture of endocrine disruptors on attention and executive functions in young children and comparing their effects with those reported in the literature.Methods Two polychlorinated biphenyls (PCBs) and 4 perfluoroalkyl substances (PFASs) were measured in the cord blood from 55 children enrolled in a longitudinal Belgian cohort study. At 6 years of age, attentional and executive functions were assessed using specific neuropsychological tests. Associations between a mixture of toxicants and cognitive performance were analyzed using the principal components approach and weighted quantile sum regression, while accounting for sex differences. Results Higher prenatal exposure to PCB mixtures was significantly associated with an increased number of omissions in the Divided Attention test. In sex-stratified analyses, this association remained significant but was observed only in boys. Additionally, boys exhibited reduced working memory and planning abilities following exposure to a mixture of PCBs and PFASs. In contrast, antenatal exposure to a mixture of PCBs and PFASs in girls was associated with reduced behavioral regulation, including inhibition control, as assessed by parent-reported questionnaires screening executive functioning in daily life. Conclusion These results support associations between antenatal exposure to a mixture of endocrine disruptors and attention and executive development, emphasizing a sex-specific effect. https://doi.org/10.1210/jendso/bvag057

Prenatal exposure to 33 endocrine-disrupting chemicals and pubertal development at age 9 in Spain,
Beneito, A., Carrizosa, C., Alvarez, O., Sarzo, B., Llop, S., Esplugues, A., Grimalt, J. O., Schettgen, T., Sakhi, A. K., Murcia, M., Freire, C., Ballester, F. and Lopez-Espinosa, M.-J., *Environmental Research*, 2026/07/01/ 2026, Vol. 301, p. 124527.

Puberty relies on a hormone-regulated cascade of events initiated in fetal life and might be disrupted by prenatal exposure to endocrine-disrupting chemicals (EDCs), with alterations manifesting during pubertal development. However, studies addressing prenatal exposure to multiple EDCs remain scarce. This study explores the associations between prenatal exposure to 33 EDCs and early sex maturation in 386 Spanish mother–child pairs (girls: 49%; recruitment: 2003–2005). We measured seven organochlorine compounds (OCs) and four perfluoroalkyl substances (PFAS) in maternal blood, and seven phenols and 15 phthalates in maternal urine. Pubertal development was assessed at age 9 using Tanner staging for genital development (GD), breast development (BD), and pubic hair

development (PH) alongside salivary sex hormones. Sex-specific analyses included single-chemical (robust Poisson/linear regression) and mixture (principal components/Bayesian kernel machine regression) analyses. In single-chemical models, higher prenatal p,p'-DDE and p,p'-DDT concentrations were associated with delayed BD and GD, respectively, while PCB-180 and parabens (ETPA, BUPA) were associated with earlier BD, and phthalates were associated with earlier PH (girls: MEHP, MEHHP, MEOHP, and MECPP; boys: MEP and MnBP). For sex hormones, β-HCH (both sexes), p,p'-DDE, PCB-180, PFOS (boys), and p,p'-DDT, OH-MPHP (girls) were positively associated with testosterone, and HCB was positively associated with estradiol (boys). Conversely, BUPA, OH-MPHP (boys), and BPA (girls) were inversely associated with testosterone. In chemical mixture models, the first component of OCs was positively associated with male testosterone, but the results of other mixture analyses were unclear. Overall, prenatal exposure to some EDCs may impair fetal programming of puberty, yet the impact of chemical mixtures remains uncertain. https://doi.org/10.1016/j.envres.2026.124527

Associations of prenatal exposure to bisphenols and phthalates with the fetoplacental ratio in the New York University Children's Health and Environment Study (NYU CHES),
Bommireddipalli, A., Erler, J. A., Nguyen, D. Q., Hyman, S., Spring, E., Medley, E. A., Kannan, K., Mehta-Lee, S. S., Trasande, L., Cowell, W. and Kahn, L. G., *Ecotoxicology and Environmental Safety*, Mar 1 2026, Vol. 312.

Fetoplacental ratio (FPR), the ratio of birthweight (BW) to placental weight (PW), indicates placental efficiency. Changes in FPR are linked to poor pregnancy outcomes and child health risks. Bisphenols and phthalates are endocrine disruptors found in plastics and personal care products that can cross the placenta and have been linked to pregnancy complications and adverse child health outcomes. We examined prenatal exposure to these chemicals in relation to FPR as a possible explanation for these risks. Our analysis included 393 participants in the New York University Children's Health and Environment Study with data on prenatal chemical exposure, BW, and PW from singleton live births. We calculated molar sums of bisphenols and of metabolites of low and high molecular weight (LMW, HMW) phthalates, diethylhexyl phthalate (DEHP), and antiandrogenic phthalates. Linear regression models were adjusted for maternal age, prepregnancy BMI, parity, gestational age at delivery, and fetal sex. Analyses were stratified by fetal sex. HMW were positively associated with FPR in the combined fetal sex sample (beta=0.26, [0.01, 0.50]) with a similar trend for DEHP and antiandrogenic phthalates (betas=0.21 [-0.04, 0.45] and 0.21 [-0.04, 0.45], respectively). Stratified analyses revealed that these results were driven by females, among whom LMW were also associated with higher FPR (beta=0.23 [0.003, 0.45]). No associations were observed between chemicals and BW in either combined or sex-stratified models. In contrast, HMW, LMW, DEHP, di-n-octylphthalate and bisphenols had negative associations with PW, suggesting placental growth as a target for phthalate-mediated endocrine disruption. https://doi.org/10.1016/j.ecoenv.2026.119925

Per- and polyfluoroalkyl substances and adolescent bone mineral density: assessing periods of susceptibility,
Buckley, J. P., Marquess, K. M., Braun, J. M., Calafat, A. M., Cecil, K. M., Chen, A., Lanphear, B. P., Wasserman, H., Xu, Y., Yolton, K. and Kuiper, J. R., *Journal of the Endocrine Society*, 2026/04/01/ 2026, Vol. 10, no. 4, p. bvag039.

Per- and polyfluoroalkyl substances (PFAS) may affect adolescent bone mineral density (BMD), but few studies have examined periods of susceptibility.To assess associations of repeated serum PFAS concentrations with early adolescent BMD.Among 218 children in a prospective pregnancy and birth cohort, we quantified serum concentrations of perfluorohexane sulfonic acid (PFHxS), perfluoroctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA) at delivery

(cord) and ages 3, 8, and 12 years. We measured BMD at 6 skeletal sites using dual-energy X-ray absorptiometry at age 12 years. We estimated covariate-adjusted differences and 95% confidence intervals (CIs) in BMD Z-scores per interquartile range (IQR) increase in each PFAS at each time point using multiple informant linear regression models. Higher PFOA concentrations were associated with lower 1/3 distal radius BMD at every time point: delivery (β: −0.39; 95% CI: −0.69, −0.10), 3 years (β: −0.36; 95% CI: −0.86, 0.14), 8 years (β: −0.54; 95% CI: −0.91, −0.16), and 12 years (β: −0.40; 95% CI: −0.75, −0.04). Higher 3-year PFHxS and PFOS concentrations were significantly associated with higher whole body, total hip, and femoral neck BMD Z-scores, while higher 12-year PFNA concentrations were associated with lower BMD Z-scores. Associations of 12-year PFAS with lower 1/3 distal radius BMD were stronger among females than males. Serum PFOA concentrations from delivery to age 12 years were associated with lower 1/3 distal radius BMD in early adolescence, while associations of other PFAS with BMD varied by exposure assessment time point, skeletal site, and sex. https://doi.org/10.1210/jendso/bvag039

Association between prenatal exposure to per- and polyfluoroalkyl substances and pubertal development in boys and girls in the Spanish INMA cohort,
Calle, S. L. D., Lertxundi, A., Alvarez, O., Lopez-Espinosa, M. J., Freire, C., Guxens, M., Schettgen, T., Le Bizec, B., Antignac, J. P., Vrijheid, M., Palacios, E. M., Cano-Sancho, G. and Irizar, A., *Environmental Research*, May 15 2026, Vol. 297.

Exposure to endocrine-disrupting chemicals (EDCs), including per- and polyfluoroalkyl substances (PFAS), has been linked to altered pubertal timing, though epidemiological findings remain inconsistent. This study examined associations between prenatal PFAS exposure and pubertal development in children. Concentrations of perfluorohexane sulfonic acid (PFHxS), perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS) and perfluorononanoic acid (PFNA) were quantified in maternal plasma collected during the first trimester of pregnancy in the Spanish INMA (Infancia y Medio Ambiente) cohort. Children's pubertal development was assessed longitudinally between ages 7 and 13 using the parent-reported Pubertal Development Scale (PDS), with specific scales for gonadal and adrenal development. Data were available for 492 mother-girls pairs at the 7- 9year follow up and 475 mother-boys pairs at the 11-13-year follow up based on the typical sex-specific timing of puberty. Poisson regression and Bayesian Kernel Machine Regression (BKMR) were used to estimate associations between PFAS (individually and as mixtures, respectively) and the risk of earlier puberty development (PDS stage 1 vs. 2+), adjusting for confounders. Among girls, PFHxS was associated with an increased risk of early adrenarche (Relative Risk [RR] = 1.85; 95% confidence interval [CI]: 1.05-3.25), while PFOS was inversely associated with early gonadarche RR = 0.61; 95% CI: 0.37-1.00). In boys, PFOS showed a marginal trend toward an increased risk of early overall pubertal onset (RR = 1.47; 95% CI: 0.99-2.19). Stratified analyses mainly revealed stronger associations among overweight/obese children. The mixture analysis suggested a positive trend for early adrenal development in both sexes, with significant associations in boys. Although our findings do not provide definitive evidence of a relationship between prenatal PFAS exposure and pubertal timing, they are compatible with the endocrine-disrupting potential of PFAS. The observed patterns, including possible modification by weight status and mixture signals, warrant further research. https://doi.org/10.1016/j.envres.2026.124095

Elevated phthalate exposure and metabolic susceptibility increased breast cancer risk: A 20-y follow-up study in Taiwan,
Chen, H.-C., You, S.-L., Lin, C.-H., Sun, C.-W., Chiang, C.-J., Yang, H.-I., Wang, L.-Y., Sun, C.-A., Liu, J., Jen, C.-L., Chen, Y.-A., Lu, Y.-S., Cheng, A.-L., Wang, S.-L., Hsiung, C. A. and Chen, C.-J., *Proceedings of the National Academy of Sciences*, 2026/03/17/ 2026, Vol. 123, no. 11, p. e2507008123.

Widely used phthalates, especially di-(2-ethylhexyl) phthalate (DEHP), increase breast cancer risk in experimental animals and humans, but long-term follow-up evidence of its human breast carcinogenicity remains inconclusive. This nested case–control study included 119 invasive breast cancer cases and 245 matched controls from a longitudinal cohort of 11,923 women recruited in 1991–1992 and followed to 2010 in Taiwan. Urine samples at baseline and follow-up visit were tested for 11 metabolites of seven phthalates using LC-ESI-MS/MS. DEHP metabolism susceptibility was evaluated by the percentage of mono-2-ethylhexyl phthalate (MEHP%) in the sum of five DEHP metabolites (∑DEHP). Odds ratios (ORs) with 95% CI from conditional logistic regression were used to examine risk predictors. DEHP was the only phthalate significantly associated with breast cancer risk. Risk increased significantly with elevated urinary levels of ∑DEHP (> 0.381 μmol/g creatinine, OR = 1.71, 95% CI = 1.02 to 2.43), MEHP (> 0.022 μmol/g creatinine, OR = 1.87, 95% CI = 1.07 to 3.25), and MEHP% (> 6.7%, OR = 1.65, 95% CI = 0.96 to 2.82). Elevated ∑DEHP and MEHP% combined with early menarche (≤ 14 years) was associated with further increased risk (OR = 7.52, 95% CI = 2.68 to 21.05). The intraclass correlation coefficient between paired baseline and follow-up samples of 152 women was 0.06 for ∑DEHP and 0.31 for MEHP%. High DEHP exposure, high MEHP%, and early menarche were associated with increased breast cancer risk. MEHP% was a better biomarker for DEHP metabolism. https://doi.org/10.1073/pnas.2507008123

Phthalates as the silent saboteurs of male fertility via changes in semen quality: a systematic review,
Dhar, S., Tomar, A., Anupama, N., Chatterjee, P. and Chatterjee, P. K., *Reproductive Biology and Endocrinology*, Mar 9 2026, Vol. 24, no. 1.

Background Phthalates, which are commonly used as plasticizers, are pervasive in modern environments. The potential effects of endocrine-disrupting chemicals (EDCs) on human reproductive health have raised concerns. Among the various health risks, a significant focus has been on male fertility, particularly the relationship between phthalate exposure and a reduced sperm count. Di-(2-ethylhexyl) phthalate (DEHP) and di-n-butyl phthalate (DBP) are two of the most studied phthalates because of their wide use in products such as plastics, cosmetics and medical devices. Growing evidence suggests that they may impair sperm production, viability, and quality, contributing to male infertility. This review synthesizes epidemiological and experimental evidence on the reproductive toxicity governed by phthalates in semen parameters. Methods This systematic review was conducted following the SWiM (synthesis without meta-analysis) guidelines. A comprehensive search across three major databases was conducted to capture literature on phthalate exposure and semen parameters, including sperm concentration, morphology and motility, published between 2014 and 14/10/2024. Two independent researchers screened and selected studies. The risk of bias in the included studies was assessed via ROBINS-E tool. A meta-analysis was not performed due to variability in the study designs. Results 38 studies met the eligibility criteria and were included in this review. Human phthalate exposure has shown that semen parameters are altered, such as a decrease in the sperm concentration. Research suggests that high exposure to phthalates such as MEHP, DEHP and DBP is associated with reduced sperm concentration, motility, and overall semen quality. Phthalates remain a potential contributing factor in male fertility issues, but the variability in findings across populations and exposure levels in these populations indicate that more research is needed to understand this relationship. Conclusion Phthalates, particularly MEHP, DEHP and DBP, negatively affect sperm concentration and affect sperm morphology, likely through endocrine disruption and impairment of testicular function via oxidative stress. The certainty of the evidence is graded as low to moderate, primarily due to the observational nature of the included studies. However, given the potential risks to reproductive health, the evidence supports a precautionary approach advocating stricter regulation of phthalate exposure in everyday products. https://doi.org/10.1186/s12958-026-01541-0

Age at menarche and exposure to non-persistent pesticides in Spanish girls from the INMA (environment and childhood) project,
Freire, C., Olivas-Martinez, A., Castiello, F., Jimeno-Romero, A., Calle, S. L. D., Suárez, B., Tardón, A., Rodriguez-Suarez, M. M., Guxens, M., Vrijheid, M., Beneito, A. and Lopez-Espinosa, M. J., *Environmental Research*, Jun 15 2026, Vol. 300.

Our objective was to assess the longitudinal association between exposure to non-persistent pesticides and the age of menarche in Spanish girls. The study was conducted in a sample of 506 girls from the INMA Project. Pesticide exposure was assessed by quantifying four insecticide metabolites (TCPy, chlorpyrifos metabolite; IMPy, diazinon metabolite; DETP, non-specific organophosphate metabolite; 3-PBA, pyrethroid metabolite) and the dithiocarbamate fungicides metabolite ethylene thiourea (ETU) in spot urine samples collected at the age of 7-10 years (2013-2016). Information on the age at menarche was collected from questionnaires completed by the girls and/or parents at successive visits from the age of 7 to 16 years. Associations between categorical exposure biomarkers and age at menarche were examined using Cox regression models adjusted for sub-cohort; maternal schooling; age, urinary creatinine, body mass index (BMI) z-score, and height of girls at the age of 7-10 years; and other pesticide biomarkers. Effect modification by BMI was also examined. Menarche was later in girls with detected versus undetected concentrations of urinary TCPy (Hazard ratio [HR] = 0.71; 95%CI = 0.54-0.92); this association was stronger among those with overweight or obesity (HR = 0.69; 95%CI = 0.47-0.99), although the interaction was not statistically significant. By contrast, menarche was earlier in girls with increasing ETU (HR = 1.32; 95%CI = 1.00-1.73 for concentrations between limit of detection and 75th percentile [P75]; HR = 1.39, 95%CI = 1.03-1.89 for concentrations > P75 versus undetected ETU); this association was stronger but not significant in girls with underweight/normal weight. These results are in line with previous findings from the INMA Project on the association of ETU exposure with earlier puberty onset in girls and provide previously unreported evidence of its association with TCPy. Further studies are needed to verify these findings and to elucidate the role of BMI in these associations. https://doi.org/10.1016/j.envres.2026.124450

Pregnancy exposure to environmental phenols and breastfeeding duration in the HOME Study,
Gerili, Z., Braun, J. M., Yolton, K., Lanphear, B., Romano, M. E., Tolstrup, J. and Timmermann, A., *International Journal of Hygiene and Environmental Health*, May 2026, Vol. 274.

Environmental phenols are endocrine-disrupting chemicals widely used in personal care products. They have been shown to affect the mammary gland, but knowledge about their impact on breastfeeding duration is limited. We aimed to explore associations between maternal phenols exposure during pregnancy and breastfeeding duration. We included 373 mother-infant pairs from the Health Outcomes and Measures of the Environment (HOME) Study (Cincinnati, Ohio, USA) enrolled from 2003 to 2006. We measured urinary concentrations of eight phenols at 16 and 26 weeks of gestation (bisphenol A, triclosan, benzophenone-3, 2,4-/2,5-dichlorophenols, methyl-/propyl-/butyl-paraben) and collected breastfeeding information until mothers reported discontinuation of exclusive and any breastfeeding. We assessed the hazard ratios (HRs) and odds ratios (ORs) of the cessation of breastfeeding in relation to the eight phenols using confounder adjusted Cox proportional hazards and logistic regression models, respectively. In adjusted Cox regression models, each doubling of urinary triclosan concentration was associated with HRs of 1.09 (95% CI: 1.00, 1.18) for any breastfeeding cessation within 6 months, and 1.08 (95% CI: 0.96, 1.21) for cessation between 6 and 12 months, with tertile-categorized analyses suggesting a dose-response relationship for cessation within 6 months. We did not observe consistent associations with breastfeeding duration for the seven other phenols, but each doubling concentrations in triclosan and BP-3 were associated with 18% (95% CI: 3, 35%) and 13% (95% CI: 1, 26%), respectively, higher odds of terminating breastfeeding

earlier than intended. Considering the limited sample size and multiple testing, our findings need to be confirmed in larger studies. https://doi.org/10.1016/j.ijheh.2026.114794

Per- and polyfluoroalkyl substances (PFAS) and miscarriage: The Norwegian Mother, Father and Child Cohort study,
Grindstad, T., Magnus, M. C., Di Nallo, A., Ramlau-Hansen, C. H., Liew, Z., Hanevik, H. I., Haug, L. S., Andersen, G. D., Rogne, T., Magnus, P., Papadopoulou, E., Håberg, S. E. and Caspersen, I. H., *Environmental Research*, Jun 1 2026, Vol. 298.

Background: Miscarriage is prevalent, occurring in around 15% of recognized pregnancies. Yet modifiable determinants remain elusive. Per- and polyfluoroalkyl substances (PFAS) can disrupt endocrine- and other biological pathways crucial for reproduction. Whether PFAS is associated with miscarriage in humans remains uncertain. Objective: To examine the association between PFAS concentrations and a recent miscarriage. Methods: We conducted a nested case-control study within The Norwegian Mother, Father, and Child Cohort Study (MoBa), which recruited pregnant women from 1999 to 2008. We utilized plasma concentrations of PFAS measured at enrolment from several MoBa sub-studies: Perfluorohexane sulfonate (PFHxS), Perfluoroheptane sulfonate (PFHpS), Perfluorooctane sulfonate (PFOS), Perfluorooctanoate (PFOA), Perfluorononanoate (PFNA), Perfluorodecanoate (PFDA) and Perfluoroundecanoate (PFUnDA). Associations with miscarriage were examined by comparing women with a single recent miscarriage to those with no prior pregnancies at enrollment, aiming to reduce the influence of parity on women's PFAS concentrations. Recency was defined as a miscarriage occurring within two calendar years before the MoBa child's birth. Logistic regression models, adjusted for age, education, and birth year, estimated associations between PFAS concentrations during the current pregnancy and recent miscarriage. The joint effect of the total PFAS mixture was evaluated using quantile-based g-computation. Results: Among 2525 nulliparous women with mid-pregnancy PFAS measurements, 253 experienced a recent miscarriage before MoBa enrolment. No clear associations between PFAS concentrations and recent miscarriage were identified in single-pollutant models nor for the overall PFAS mixture (OR 0.95 (95 % CI: 0.83-1.09, per quartile increase in PFAS). Additional adjustments for potential confounding factors, including body mass index, menstrual cycle characteristics and use of oral contraceptives did not alter the observation of overall nullfindings. https://doi.org/10.1016/j.envres.2026.124276

Sex-specific associations of prenatal and postnatal exposure to 15 endocrine-disrupting chemical exposures with visual impairment at age three: the Korean Children's Environmental Health Study (Ko-CHENS),
Ham, D., Kim, S. Y., Bae, S. and Ko, C. S. G., *Environment International*, Apr 2026, Vol. 210.

Background Endocrine-disrupting chemicals (EDCs) have been linked to pediatric outcomes, but evidence on visual development and sex differences is scarce. We examined whether prenatal and postnatal EDC exposures were associated with visual impairment at age 3. Methods Participants were drawn from the Korean Children's Environmental Health Study, with urinary biomarkers measured at early pregnancy (n = 340), late pregnancy (n = 454), 24 months (n = 344), and 36 months (n = 713). A subset with complete data at all windows (n = 115) was analyzed using generalized estimating equations. Fifteen biomarkers (phthalate metabolites, bisphenols, parabens, triclosan) were assessed, and logistic regression models with inverse probability weighting estimated window-specific and population-averaged effects. Mixture effects were evaluated using weighted quantile sum regression and quantile g-computation. Visual acuity at 36 months was measured on the decimal scale, with impairment primarily defined as <0.5 in either eye, alongside alternative definitions for robustness. Results Girls showed more consistent adverse associations between higher EDC concentrations and increased impairment risk. Each unit increase in mono-(3-carboxypropyl)

phthalate was associated with higher odds of impairment during late pregnancy (OR = 2.47, 95% CI: 1.97, 3.12), at 24 months (OR = 1.64, 95% CI: 1.38, 1.95), and at 36 months (OR = 1.36, 95% CI: 1.14, 1.61), while bisphenol A at 36 months also conferred elevated risk (OR = 1.48, 95% CI: 1.32, 1.67). Boys generally exhibited weaker or inverse associations, except for mono-(carboxyoctyl) phthalate at 24 months (OR = 1.34, 95% CI: 1.19, 1.52). Mixture models were largely null, though weights consistently highlighted phthalates. Conclusions Early-life EDC exposures were associated with visual impairment at age 3 in a sex-specific manner, with stronger and more consistent effects in girls. https://doi.org/10.1016/j.envint.2026.110194

Associations of urinary and follicular fluid phthalate exposure with salpingitis in women seeking fertility treatment,
Hou, Q. Q., Liao, H. M., Zhang, Z. M., Yuan, J. Y., Guo, Q. C., Wang, Y., Li, J., Du, Y. Y., Zeng, Q., Deng, T. R. and Li, Y. F., *Environmental Pollution*, Jun 1 2026, Vol. 398.

Endocrine-disrupting chemicals are recognized for their impact on fallopian tube function; however, epidemiological evidence linking phthalates to fallopian tube disorders is still limited. In this cross-sectional study within the Tongji Reproductive and Environmental (TREE) Cohort, we collected urine and follicular fluid (FF) samples from 291 infertile women aged 20 to 45 years with no history of sexually transmitted infections (STIs) or pelvic inflammatory disease (PID), and measured eight phthalate metabolites. Salpingitis cases (n = 62) were identified based on clinical diagnosis documented in medical records. Notably, residual confounding by STI/PID-related factors may still exist despite this exclusion. We evaluated associations with individual metabolites and mixtures using logistic regression, Bayesian kernel machine regression (BKMR), and weighted quantile sum (WQS) regression models. In both crude and adjusted models, higher tertiles of monobenzyl phthalate (MBzP) in FF were positively associated with salpingitis (P for trend = 0.04). Upon adjusting for covariates, a per logarithm (ln)-unit rise in mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) levels in FF was linked to a 1.63-fold elevation (95% CI: 1.01, 2.64) in salpingitis odds. Furthermore, concentrations of monoethyl phthalate (MEP) in urine samples were positively correlated with salpingitis [adjusted model: 1.38 (1.06, 1.80)]. Additionally, the mixtures of phthalate metabolites in both urine and FF generally did not show significant associations with salpingitis. Stratified analyses revealed an increased odds of salpingitis associated with urinary mono(2-ethyl-5carboxypentyl) phthalate (MECPP) in women under 30 years of age (P for interaction = 0.03), with urinary MBzP in women with body mass index (BMI) >= 24 kg/m2 and non-female factor infertility (P for interaction = 0.01), and with FF mono(2-ethyl-5-oxohexyl) phthalate (MEOHP) in the female-factor infertility group (P for interaction = 0.02). These results indicate that certain phthalate metabolites in FF and urine show a positive correlation with salpingitis, underscoring the necessity for further research. https://doi.org/10.1016/j.envpol.2026.128057

Preterm birth attributable to exposure to chemicals used in plastic materials: a global estimate,
Hyman, S., Acevedo, J. and Trasande, L., *eClinicalMedicine*, 2026/04/01/ 2026, Vol. 94.

Phthalates, widely used as plasticizers, have been associated with adverse pregnancy outcomes, including preterm birth (PTB). This analysis quantifies the global burden of PTB associated with exposure to di (2-ethylhexyl) phthalate (DEHP) and diisononyl phthalate (DINP). A disease burden model was constructed using 2018 exposure estimates from available population-level biomonitoring surveys and meta-analyses in regions lacking such surveys. Hazard ratios (HRs) for PTB associated with phthalate exposure were derived from a previous cohort study and applied to regional exposure distributions, and a search from 2016 to 2026 was completed to identify uncertainty intervals for effect estimates. PTB-attributable outcome estimates were obtained from the Institute for Health Metrics and Evaluation's. Phthalate-associated PTB outcomes were calculated using a population

attributable fraction approach. In 2018, 1.97 million DEHP-attributable PTBs (8.74% of global PTBs) were estimated, alongside 74,000 deaths, 6.69 million years of life lost (YLLs) and 1.22 million years of life lived with disability (YLDs). 1.93 million of these incident PTBs, 72,500 deaths, 6.56 million YLLs, and 1.20 million YLDs could be linked to plastics. The highest absolute burden was estimated in the Middle East and South Asia, representing over 54% of estimated attributable PTBs, followed by Africa at 26%. Attributable morbidity and mortality trends differed in accordance with underlying regional patterns of burden. Estimates were similar for DiNP (64,000 deaths, 1.88 million PTB cases, 5.77 YLLs, 1.35 YLDs, and PAF of 8.32%). To account for uncertainties in extrapolating effect estimates from the US, effect estimates from four previous global meta-analyses were also used to calculate uncertainty intervals. Uncertainty intervals revealed as low as 4 times lower estimates for DEHP, and 10 times lower DiNP estimates, highlighting the need for further investigation to refine DiNP associated morbidity and mortality.
This model presents the first global estimate of the PTB burden linked to exposure to certain phthalates. Burden was estimated to be disproportionate in South Asia, the Middle East, and Africa. Implementing regulatory measures to limit exposure to phthalates as a class could help reduce the global PTB burden, particularly in and areas with high PTB risk, limited regulations, and growing plastics industries. https://doi.org/10.1016/j.eclinm.2026.103842

Exploring the hidden cause of assisted reproductive technologies unfavorable outcomes through the biomonitoring study of heavy metals exposure among women,
Ilincic, M., Milosevic, N., Milanovic, M., Sazdanic-Velikic, D., Spanovic, M., Bjelica, A. and Milic, N., *Journal of Trace Elements in Medicine and Biology*, Jun 2026, Vol. 95.

Background: Endocrine disrupting metals such as cadmium (Cd), lead (Pb) and mercury (Hg) may have significant influence on fertility issues among otherwise healthy women. Methods: In this study, fifty women with preserved ovarian function, undergoing in vitro fertilization (IVF) procedure were tested for heavy metals (Cd, Hg and Pb) in their morning urine samples using inductively coupled plasma mass spectrometry after microwave digestion. Results: None of the women had measurable lead in the urine samples while cadmium and mercury were quantified in 28% and 60% of the samples, respectively. Serum LH levels were significantly lower (p = 0.046) among women with measurable urinary cadmium values compared to those with cadmium below the limit of quantification (LOQ). The number of immature oocytes retrieved during transvaginal aspiration was significantly higher (p = 0.030) in women with mercury above LOQ in comparison to those below LOQ. The elevation of urinary mercury concentrations was followed by the increment AST and ALT (p = 0.035 and p = 0.001, respectively). Moreover, higher urinary mercury levels were positively associated with fasting and 2 h post-load serum glucose levels during oral glucose tolerance testing (p = 0.035 and p = 0.002, respectively). For the first time, statistically significant (p = 0.009) correlation was obtained between the urinary mercury concentration and serum LDH values. All the associations between mercury and the observed parameters remained significant after adjustments for age, BMI and time attempting to conceive were made. Conclusions: Women undergoing IVF have considerable amount of cadmium and mercury in the urine samples, despite the absence of occupational exposure. https://doi.org/10.1016/j.jtemb.2026.127858

Age-Specific Association Between Urinary Phthalate Metabolites and Diabetes Mellitus: Findings from the Korean National Environmental Health Survey Cycle 4 (2018-2020),
Lee, J. E., Lee, G. T. and Cho, H. A., *Healthcare*, Mar 5 2026, Vol. 14, no. 5.

Highlights What are the main findings? Urinary phthalate metabolites showed distinct association with diabetes mellitus across age groups, indicating substantial age-related heterogeneity. MnBP and MEP emerged as key metabolites, with a strong association in young and older adults, whereas their

effects in middle-aged adults were more moderate. What are the implications of the main findings? Age should be considered an effect modifier, rather than merely a covariate, in environmental diabetes research. Age-tailored exposure prevention and surveillance strategies may enhance the effectiveness of diabetes prevention efforts. Highlights What are the main findings? Urinary phthalate metabolites showed distinct association with diabetes mellitus across age groups, indicating substantial age-related heterogeneity. MnBP and MEP emerged as key metabolites, with a strong association in young and older adults, whereas their effects in middle-aged adults were more moderate. What are the implications of the main findings? Age should be considered an effect modifier, rather than merely a covariate, in environmental diabetes research. Age-tailored exposure prevention and surveillance strategies may enhance the effectiveness of diabetes prevention efforts. Abstract Background/Objectives: Phthalates are encountered in everyday consumer and indoor environments, and their metabolites are commonly detected in urine. Although phthalate exposure has been linked to diabetes mellitus (DM), associations may vary by life stage. Therefore, we evaluated age-specific association between urinary phthalate metabolites and DM using nationally representative Korean data. Methods: We conducted a cross-sectional analysis of the Korean National Environmental Health Survey Cycle 4 (2018-2020). Adults aged >= 19 years with complete data were included. Eight urinary metabolites were evaluated. Metabolites were log-transformed, and those showing interaction were analyzed by tertiles. Complex survey-weighted logistic regression estimated odds ratios (95% confidence intervals) for DM, adjusting for demographic, socioeconomic, and health behavior factors. Analyses were stratified by age group. Results: Geometric mean (GM) concentrations among participants with DM varied significantly by age groups for several metabolites. Interaction analyses identified statistically significant effects for selected phthalate metabolites, including MnBP, MCPP, and MEP. In the age-stratified adjusted models, MnBP and MCPP were more strongly associated with DM in young adults, whereas the pattern for MEP appeared more evident in older adults, suggesting potential life-course differences in metabolic vulnerability. Conclusions: Associations between urinary phthalate metabolites and DM vary substantially by age, indicating life-course differences in exposure pathways and metabolic vulnerability. Age-specific prevention and surveillance strategies may improve environmental health interventions for DM. https://doi.org/10.3390/healthcare14050655

Exposure to phthalate and phenol mixtures and obesity in children and adolescents: the dominant role of bisphenol A,
Liu, F. Q., Li, Y., Kong, B. X., Liang, C. H., Chen, L., Xiong, J. F., Zhao, X., Su, Z., Xiao, P., Mi, J., Yao, P., Tang, Y. H. and Li, Y. Y., *Lipids in Health and Disease*, Mar 17 2026, Vol. 25, no. 1.

Background Little research has explored the association of exposure to phthalates and phenols with obesity in Chinese children and adolescents, especially with regard to co-exposure. The mechanisms by which exposure to phthalates or phenols contributes to obesity in children and adolescents remain unclear. Therefore, this case-control study was aimed at examining the effects of multiple phthalate and phenol exposures on obesity and further exploring the potential key role of insulin. Methods The cross-sectional study involved 293 pairs of children and teenagers with obesity and normal weight matched on age (+/- 1 year) and sex. In addition, 21 urinary endocrine-disrupting chemicals (EDCs), including 11 phthalate metabolites and 10 phenols, were measured. The associations of individual EDCs and EDC mixtures with obesity were investigated using conditional logistic regression models, weighted quantile sum (WQS) analyses, and Bayesian kernel machine regression (BKMR). Mediation analyses were performed to evaluate the mediated effects of insulin on the relationships between EDCs and obesity. Results In the single-EDC model, the highest quartiles of mono-iso-butyl phthalate (MiBP), mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-carboxymethylhexyl phthalate (MCMHP), and bisphenol A (BPA) were positively associated with obesity compared to their lowest quartiles. In mixed-exposure analyses, the WQS and BKMR model results consistently suggested that

exposure to phthalate and phenol mixtures showed a positive association with obesity. BPA was identified as an essential exposure in the mixture with dominant effects on obesity in children and adolescents. Further mediation analysis revealed that insulin partly mediated the relationship between BPA and obesity, with the proportion of mediation at 50.13%. Conclusions These findings suggested that exposure to phthalates and phenols, either alone or in mixtures, was significantly linked to childhood obesity. The obesogenic effect of exposure to BPA in children and adolescents deserves further attention, which may be mediated by insulin in part. https://doi.org/10.1186/s12944-026-02903-8

The association between PFAS exposure, menstrual cycle parameters, and reproductive hormones in adolescent girls,
Malave-Ortiz, S., Mcneley, S. a. M., Denslow, S., Bangma, J., Ferguson, K. K., Fenton, S. E. and Shaw, N. D., *Journal of Clinical Endocrinology & Metabolism*, 2026.

Context Perfluoroalkyl and polyfluoroalkyl substances (PFAS), sometimes referred to as "forever chemicals", are widespread. Certain PFAS exposures have been associated with reproductive abnormalities in women, but limited data exist in adolescents. Objective To investigate the relationship between PFAS, menstrual cycle length/variability, and reproductive hormones in adolescents.Methods Thirty-eight girls completed menstrual diaries and contributed daily urine samples to measure creatinine (Cr)-corrected luteinizing hormone (LH), estrone-3-glucuronide (E1G), and pregnanediol-3-glucuronide (PdG). Twenty-four PFAS were measured (n = 88 serum samples, average 2.32 samples/participant over the course of 1.20 +/- 1.34 years) using mass spectrometry. Linear mixed-effects models were used to assess associations between PFAS and total cycle, follicular phase, and luteal phase lengths and hormone levels. Models were performed unadjusted and adjusted for gynecologic age, body fat percent, and race/ethnicity.Results Participants were 12.8 +/- 1.0 years old (mean +/- SD) with a gynecologic age of 0.3 +/- 0.2 years. Most were non-Hispanic White and of normal weight. Four PFAS were consistently detected: perfluorobutanesulfonic acid (PFBS), perfluorohexanesulfonic acid, perfluorooctanoic acid, and perfluorooctanesulfonic acid. There were no associations between PFAS and cycle length or variability. PFBS was positively associated with peak E1G levels (beta = .15, 95% CI [0.00, 0.29], P = .049), but no species was associated with peak LH or PdG levels. Conclusion PFAS were widely detected in healthy girls. PFBS was positively associated with E1G levels, suggesting potential ovarian effects. Analyses are ongoing to understand PFAS exposure sources and to determine if ongoing exposure may impact reproductive health. Clinical trial information Clinicaltrials.gov registration number: NCT02583646. https://doi.org/10.1210/clinem/dgag148

Exposure to organophosphate esters and trajectories of gestational weight gain: A large prospective cohort study,
Martin, B., Cantonwine, D. E., Meeker, J. D., Ospina, M., Calafat, A. M., Mcelrath, T. F., Ferguson, K. K. and Welch, B. M., *Environmental Research*, Jun 15 2026, Vol. 300.

Background: Organophosphate esters (OPEs) can be used as flame retardants and plasticizers in consumer products. Gestational exposure may disrupt maternal metabolic function, which is dynamic during pregnancy. Gestational weight gain (GWG) serves as an important indicator of maternal metabolic health. We aimed to determine prospective associations between biomarkers of maternal OPE exposure and GWG. Methods: Concentrations of five OPE biomarkers were measured across repeated urine samples in the LIFECODES Fetal Growth Study (n = 901, 2008-2018) and evaluated as pregnancy-averaged values. Maternal weight gain was calculated from repeated weight measures (median = 14/participant) and mixed-effects modeling was applied to predict maternal weight at delivery. Total GWG, the primary outcome, was calculated by the difference between predicted

weight at delivery and self-reported pre-pregnancy weight. Linear regression models estimated associations between individual biomarkers and total GWG. Group-based trajectory models were used to identify three trajectories of GWG (i.e., low-catch up, expected, constant-high), and associations between OPEs and trajectory membership were estimated using multinomial regression models. Results: We observed mixed associations between OPE biomarkers and GWG. For example, a doubling in bis(2-chloroethyl) phosphate was associated with 0.14 kg lower (95% confidence interval [CI]:-0.26, 0.01) GWG, whereas a doubling in diphenyl phosphate (DPHP) was associated with 0.16 kg greater (95% CI:-0.08, 0.46) GWG; however, both confidence intervals included the null. Among GWG trajectories, a doubling in DPHP was associated with higher odds of being in the constant-high GWG trajectory (early rapid, sustained weight gain) compared to the expected group (odds ratio: 1.28, 95% CI: 0.98, 1.69). Conclusions: This study provides novel evidence that certain OPE exposures may not only influence women's total weight gain during pregnancy, but the trajectory in which that weight gain occurs. https://doi.org/10.1016/j.envres.2026.124434

Associations of Urinary Metabolites of Parabens and Bisphenol a with Premature Thelarche among a Sample of Iranian Girls,
Mozafarian, N., Hashemipour, M., Maracy, M. R., Galehdari, H. and Kelishadi, R., *Journal of Clinical Research in Pediatric Endocrinology*, Mar 2026, Vol. 18, no. 1, p. 85-96.

Objective: Endocrine-disrupting chemicals may influence the process of puberty including the development of premature thelarche (PT). Our aim was to investigate the relationship between exposure to bisphenol A (BPA) and parabens with PT among a sample of Iranian girls. Methods: This case-control study was conducted in 2022-2023 on girls with a mean (standard deviation) age of 7.5 (0.6) years in Isfahan, Iran. Participants were 90 newly diagnosed PT cases and 114 healthy controls. Spot urine samples were collected from both groups to measure the levels of BPA and paraben metabolites. Analyses of BPA and paraben metabolites included methyl paraben (MeP), ethyl paraben (EtP), propyl paraben, and butyl paraben and benzyl paraben and were performed by gas chromatography-mass spectrometry. The association between concentrations of creatinine-standardized urinary BPA and parabens and PT was analyzed with multiple logistic regression models, after adjusting for potential confounders. Results: The results showed that individuals in the highest quartile of MeP [odds ratio (OR)=4.3, 95% confidence interval (CI): 1.2-14.9, p=0.023], EtP (OR=4.7, 95% CI: 1.3-17.2, p=0.018) and BPA (OR=5.03, 95% CI: 1.4-17.9, p=0.013) had a significantly higher odds for PT compared to those in the lowest quartile. Conclusion: The findings of this study suggest that exposure to BPA, MeP and EtP is related to increased odds of early breast development in girls. Limiting the exposure to these chemicals may help to reduce the risk of PT. https://doi.org/10.4274/jcrpe.galenos.2025.2025-3-22

Exposure to Obesogenic Endocrine Disruptors in Childhood. Impact on Biomarkers of Metabolic Status,
Nso-Roca, A. P., Tortajada-Genaro, L. A., Pons-Fernández, N. and Sánchez-Ferrer, F., *Exposure and Health*, Mar 18 2026, Vol. 18, no. 2.

Childhood obesity is an escalating global health concern, partly driven by environmental factors such as endocrine disruptors (EDs), which can alter metabolism and promote adiposity. This cross-sectional study examined exploratory associations between exposure to obesogenic EDs (bisphenols, parabens and benzophenones) and body composition in 72 children aged 3 to 15 years (53 with obesity and 19 normal-weight controls) recruited from two hospitals in Spain. Metabolic status, body composition and urinary levels of EDs were evaluated using tandem mass spectrometry. The findings, which are pioneering in evaluating multiple exposure to chemicals, identify exploratory associations between the presence of EDs in 100% of the participants, with parabens the most frequently detected. Higher

methylparaben levels were observed in the group with obesity. Correlational analyses revealed positive associations between specific EDs and adiposity parameters, including triponderal mass index and visceral fat percentage. These results suggest a potential link between exposure to EDs and the development of childhood obesity. The massive and early exposure to EDs underscores the urgent need for preventive policies and longitudinal studies to evaluate their effects. These preliminary findings provide exploratory insights for developing effective strategies to combat childhood obesity. https://doi.org/10.1007/s12403-026-00764-1

Association of exposure to synthetic phenols and metal(loid)s with early puberty in Spanish girls: a multicentric case-control study,
Olivas-Martinez, A., Escribano, A., Riaño-Galán, I., Torrebias, M., Olmedo, P., Gil, F., Suarez, B., Rodríguez-Carrillo, A., Corripio, R., Castiello, F., Bosch, M. Z., Herrero, X., Ventura-Wichner, P. S. and Freire, C., *European Journal of Pediatrics*, Apr 24 2026, Vol. 185, no. 5.

The incidence of precocious puberty (PP) and its variants in girls has increased over recent decades. Early-life exposure to endocrine disrupting chemicals (EDCs) may contribute to this trend. The purpose of this study is to investigate the association of exposure to several phenolic EDCs and metal(loid)s, both individually and as a mixture, with the risk of early puberty in Spanish girls. This multicentric case-control study recruited 182 girls aged 4-8 years diagnosed with PP (n = 101) or manifesting any sign of early puberty (premature thelarche: n = 74, other: n = 7) and 128 controls in six Spanish hospitals. Bisphenol, paraben, benzophenone (BzP), and metal(loid) concentrations were quantified in spot urine samples. Adjusted logistic regression and quantile g-computation models were used to assess associations of individual chemicals and their mixture, respectively, with risk of early puberty. Increased bisphenol A (BPA) exposure was associated with higher risk of overall early puberty [OR (95% CI) = 1.44 (1.19 - 1.73) per two-fold increase in urinary concentrations], PP [1.69 (1.26 - 2.27)], and premature thelarche [1.29 (1.05 - 1.58)]. Higher total BzPs (3rd tertile) and zinc (Zn) concentrations were also associated with higher risk of early puberty and PP. The mixture showed a significant effect on the risk of overall early puberty [OR (95% CI) = 1.20 (1.04 -1.38)], primarily driven by BPA.Conclusion: These findings suggest that exposure to BPA and BzPs may increase the risk of early puberty in girls. Longitudinal studies are warranted to confirm these findings. What is Known:center dot Exposure to endocrine disrupting chemicals (EDCs), such as bisphenol A (BPA), may accelerate or delay puberty onset, but evidence remains limited and inconsistent.center dot Toxic metals with estrogenic properties such as cadmium have been poorly studied in relation to puberty timing.What is New:center dot Higher BPA, benzophenones, and Zn levels were associated with greater odds of early puberty, including PP and premature thelarche, in Spanish girls.center dot Mixture analysis indicated a significant combined effect on early puberty risk, mainly driven by BPA.AbstractThe incidence of precocious puberty (PP) and its variants in girls has increased over recent decades. Early-life exposure to endocrine disrupting chemicals (EDCs) may contribute to this trend. The purpose of this study is to investigate the association of exposure to several phenolic EDCs and metal(loid)s, both individually and as a mixture, with the risk of early puberty in Spanish girls. This multicentric case-control study recruited 182 girls aged 4-8 years diagnosed with PP (n = 101) or manifesting any sign of early puberty (premature thelarche: n = 74, other: n = 7) and 128 controls in six Spanish hospitals. Bisphenol, paraben, benzophenone (BzP), and metal(loid) concentrations were quantified in spot urine samples. Adjusted logistic regression and quantile g-computation models were used to assess associations of individual chemicals and their mixture, respectively, with risk of early puberty. Increased bisphenol A (BPA) exposure was associated with higher risk of overall early puberty [OR (95% CI) = 1.44 (1.19 - 1.73) per two-fold increase in urinary concentrations], PP [1.69 (1.26 - 2.27)], and premature thelarche [1.29 (1.05 - 1.58)]. Higher total BzPs (3rd tertile) and zinc (Zn) concentrations were also associated with higher risk of early puberty and PP. The mixture showed a significant effect on the risk of overall early puberty [OR (95% CI) = 1.20 (1.04 -1.38)], primarily driven

by BPA.Conclusion: These findings suggest that exposure to BPA and BzPs may increase the risk of early puberty in girls. Longitudinal studies are warranted to confirm these findings. What is Known:center dot Exposure to endocrine disrupting chemicals (EDCs), such as bisphenol A (BPA), may accelerate or delay puberty onset, but evidence remains limited and inconsistent.center dot Toxic metals with estrogenic properties such as cadmium have been poorly studied in relation to puberty timing.What is New:center dot Higher BPA, benzophenones, and Zn levels were associated with greater odds of early puberty, including PP and premature thelarche, in Spanish girls.center dot Mixture analysis indicated a significant combined effect on early puberty risk, mainly driven by BPA. https://doi.org/10.1007/s00431-026-06919-1

Per- and Polyfluoroalkyl Substances and Endometriosis: A Systematic Review and Meta-Analysis, Pilling, S., Mitchell, K. and Ramdass, P. V. a. K., *Toxics*, 2026/04// 2026, Vol. 14, no. 4, p. 337.

Per- and polyfluoroalkyl substances (PFASs) are persistent endocrine-disrupting chemicals implicated in reproductive dysfunction. Epidemiologic evidence examining their association with endometriosis remains inconsistent. Thus, we conducted a PRISMA-compliant systematic review and meta-analysis using PubMed, Embase, EBSCO Host, and Google Scholar databases. RStudio software was used for all analyses. Random-effects or fixed-effects model was applied to estimate pooled odds ratios (ORs) and standardized mean difference (SMD) in PFAS levels between endometriosis patients and controls. Heterogeneity was assessed using I2 statistics. Publication bias was evaluated using funnel plots, and Egger's and Begg's tests. Twelve studies met the inclusion criteria for the systematic review and eleven were included in the quantitative synthesis. Overall, PFSAs (OR: 1.50; 95% CI: 1.12–2.00) and PFCAs (OR: 1.46; 95% CI: 1.12–1.90) were significantly associated with increased odds of endometriosis, particularly PFOS and PFOA. However, analyses of pooled SMD did not demonstrate consistent concentration differences between endometriosis cases and controls. Heterogeneity was moderate to high for most compounds. Funnel plot symmetry and Egger's and Begg's tests suggest no publication bias. Exposure to PFASs, particularly PFOS and PFOA, may be associated with increased odds of endometriosis. Further prospective studies incorporating mixture modeling and emerging PFASs are warranted. https://doi.org/10.3390/toxics14040337

A prospective study of per- and polyfluoroalkyl substances (PFAS), stress, and birth size in a cohort of US Black women,
Schildroth, S., Henn, B. C., Lovett, S. M., Wesselink, A. K., Nillni, Y. I., Heiger-Bernays, W., Harmon, Q. E., Vines, A. I., Baird, D. D. and Wise, L. A., *Environmental Health*, Feb 27 2026, Vol. 25, no. 1.

Background Per-and polyfluoroalkyl substances (PFAS) and psychosocial stress can dysregulate hormonal processes underlying fetal growth. Less is known about the effect of co-exposure to PFAS and stress on birth size. Objective We investigated associations of a preconception mixture of PFAS with birth size and assessed effect modification by perceived stress.Methods We used prospective data from 321 participants from the Study of Environment, Lifestyle, and Fibroids, a cohort of 23-35-year-old women from Detroit, MI who identified as Black/African American. We quantified plasma concentrations of six PFAS in baseline blood samples using online solid-phase extraction-liquid chromatography-isotope dilution tandem mass spectrometry. We assessed experience of perceived stress at baseline using the Perceived Stress Scale-4. Participants reported intervening pregnancies at follow-up visits (at similar to 20, 40, and 60 months). We calculated sex-standardized birthweight-for-gestational-age (BW-for-GA) z-scores from reported birthweight and gestational age at delivery. We employed Bayesian Kernel Machine Regression to estimate associations ((3s, with 95% credible intervals [CrI]) of the PFAS mixture with BW-for-GA z-scores and assess effect modification by stress scores, adjusting for confounders. Results The 90th percentile of the mixture (vs. 50th percentile) was weakly associated with higher BW-for-GA z-scores (beta = 0.37, 95% CrI=-0.20, 0.95), driven by

perfluorohexanesulfonic acid (PFHxS) and stress scores. PFHxS was weakly associated with higher BW-for-GA z-scores, and this association was stronger at higher levels of perceived stress. Conclusion A mixture of PFAS and stress scores was weakly associated with higher BW-for-GA z-scores in a cohort of Black women, with evidence of a PFHxS-stress score interaction. https://doi.org/10.1186/s12940-026-01279-7

Joint effects of prenatal endocrine disrupting chemicals and heavy metal mixture on birth size and maternal complication in the Korea children's environmental health cohort study,
Shim, S. R., Moon, N. and Kim, J. H., *Environmental Research*, Jun 15 2026, Vol. 299.

Background: Prenatal exposure to mixtures of heavy metals and endocrine-disrupting chemicals (EDCs) may adversely affect birth outcomes, but their joint effects remain understudied. Methods: This study analyzed 4715 Korean mother-infant pairs from the Ko-CHENS cohort. Maternal whole blood was used to measure three heavy metals (lead, cadmium, mercury), while urine samples were collected to quantify 15 non-persistent EDCs, including phthalate metabolites, bisphenols, and parabens. Birth size was assessed using INTERGROWTH-21st z-scores. Weighted Quantile Sum (WQS) regression and Bayesian Kernel Machine Regression (BKMR) were applied to evaluate mixture effects. Results: Individual chemical analyses revealed significant negative associations between birth weight and MEOHP ((3 =-0.146, p = 0.034), MCOP ((3 =-0.057, p = 0.023), MtP ((3 =-0.032, p = 0.021), and Cd ((3 =-0.141, p = 0.023). Birth length showed similar patterns with MEOHP and MCOP. Weight-for-length was negatively associated with BPS ((3 =-0.100, p = 0.008) and Pb ((3 =-0.253, p = 0.048). WQS analysis demonstrated significant negative mixture effects on birth length ((3 =-0.052, p = 0.040) and weight-for-length ((3 =-0.108, p = 0.017). BKMR revealed threshold-dependent relationships, with adverse effects becoming significant when exposure levels exceeded the 50th percentile. Heavy metals emerged as primary drivers of mixture effects, while subgroup analyses showed no significant effects from phthalate or phenol mixtures alone. Conclusions: Prenatal exposure to environmental chemical mixtures significantly reduces birth size through threshold-dependent mechanisms. Heavy metals are key contributors to adverse mixture effects, highlighting the need for cumulative risk assessment approaches in environmental health policy. https://doi.org/10.1016/j.envres.2026.124368

Exposure to Endocrine Disruptors and Stress Hormones Across Pregnancy Trimesters: Links with Maternal Telomere Length,
Vakonaki, E., Hatzidaki, E., Baliou, S., Marmara, M., Alegakis, A., Mylonaki, E., Volonaki, Z., Makrygiannakis, F., Tsatsakis, A. and Tzatzarakis, M. N., *Journal of Xenobiotics*, 2026/06// 2026, Vol. 16, no. 3, p. 82.

Background: Exposure of pregnant women to stress and endocrine-disrupting chemicals (EDCs) during pregnancy can have a substantial impact on mother and infant health. We investigated the concentrations of EDCs, such as parabens (PBs) and triclosan (TCS), as well as stress hormones (cortisone and cortisol), across pregnancy trimesters and examined their associations with maternal average telomere length (TL). Methods: Hair samples from 49 postpartum women were analyzed using liquid chromatography–mass spectrometry (LC-MS) to quantify EDCs and stress hormone concentrations. Results: The mean methyl paraben concentrations in the hair of postpartum women were prevalent across all pregnancy trimesters, while butyl paraben was detected at the lowest levels. The mean concentration of PBs followed the order methyl > propyl > ethyl > benzyl > butyl paraben across pregnancy trimesters. We found that ethyl paraben and triclosan were each positively and significantly associated with cortisol levels in postpartum women's hair. Consistent with this, the mean cortisone concentration gradually increased from the first to the third pregnancy trimester, whereas cortisol reached the highest mean concentration at the second trimester. A significant

positive association between cortisol and cortisone levels was observed. Further analyses revealed that mothers' average TL was positively associated with ethylparaben and triclosan levels and inversely associated with benzylparaben levels. Last but not least, we found that cortisol/cortisone levels were positively associated with postpartum women's TL in a statistically significant manner. Conclusions: In the present study, prenatal exposure to stress hormones and EDCs appears to exert a statistically significant impact on maternal TL dynamics. https://doi.org/10.3390/jox16030082

Fetal exposure to bisphenols and phthalates and risk of respiratory conditions in infancy. The Generation R Next Study,
Varma, P., Karramass, T., Trasande, L., Ferguson, K. K., Kannan, K., Sakhi, A. K., Jaddoe, V. W. V. and Duijts, L., *Environmental Research*, Jun 15 2026, Vol. 299.

Fetal exposure to bisphenols and phthalates may lead to alterations in the development of the respiratory and immune systems in children, subsequently increasing their susceptibility to respiratory conditions in infancy. We aimed to study the associations of fetal exposure to bisphenol and phthalate metabolites with the risk of respiratory conditions in infancy. This study, involving 1295 mother-child pairs, was embedded in a populationbased prospective cohort in Rotterdam, the Netherlands. We measured maternal concentrations of bisphenols and phthalate metabolites in spot urine samples collected during the first and third trimesters of pregnancy. The ever occurrence and number of episodes of asthma-related symptoms and respiratory tract infections were assessed at ages 6 and 12 months using ISAAC-based questionnaires. The pregnancy-averaged and trimesterspecific urinary bisphenol and phthalate metabolite concentrations were not associated with the ever occurrence of wheezing, shortness of breath, or upper or lower respiratory infections in the first year of life. However, a doubling in the pregnancy-averaged urinary concentrations of Bisphenol F (BPF), Bisphenol S (BPS), and certain high molecular weight (HMW) phthalates was associated with 1 to 3 or 4 and more episodes of asthmarelated symptoms in the first year of life (range odds ratio (OR) [95% confidence interval]: 1.04 [1.01, 1.06] to 1.35 [1.22, 1.49]). A mixture of pregnancy-averaged bisphenol and phthalate concentrations was not associated with any of the respiratory conditions. To conclude, fetal exposure to bisphenols, phthalates or their mixtures was not associated with ever occurrence of respiratory conditions in infancy. However, higher levels of BPF, BPS and certain HMW phthalates may increase the number of episodes of asthma-related symptoms in infancy. https://doi.org/10.1016/j.envres.2026.124304

Preliminary Evidence of Microplastics in the Human Thyroid and Their Potential Association with Autoimmune Thyroiditis,
Yu, S. T., Fu, J. R., Fan, Z. H., Ye, Q. T., Zhang, S. L. and Guan, H. X., *Thyroid*, 2026.

Background: Microplastics (MPs) have been identified in multiple human tissues and are increasingly implicated in systemic health risks. Their presence in the thyroid gland, however, remains unexamined. Autoimmune thyroiditis (AIT) is the most frequent autoimmune thyroid disorder and the leading cause of hypothyroidism. This study aims to detect the presence of MPs in the thyroid and their potential relevance to AIT. Methods: In this case-control study, thyroid tissues were obtained from 29 patients with histologically confirmed AIT and 29 age- and sex-matched non-AIT controls who underwent thyroidectomy due to thyroid nodules. MP burden was quantified by pyrolysis-gas chromatography-mass spectrometry (Py-GC/MS). Particle-level polymer identity and particle characteristics, including size, shape, and color, were assessed using micro-Raman spectroscopy, whereas scanning electron microscopy (SEM) was employed for morphological observation. Results: MPs were detected in thyroid tissues from both groups. Py-GC/MS revealed significantly higher total MP concentrations in the AIT group compared to controls (median: 19.9 vs. 1.9 mu g/g; p=0.012). This elevation was primarily driven by polyvinyl chloride (PVC), which was significantly higher in AIT

patients. Micro-Raman spectroscopy identified particles ranging from 33.9 to 1467 & micro;m. The AIT group contained significantly increased MPs abundance compared with the non-AIT control group (172 vs. 50.2 items/g, p=0.037). Morphological profiling revealed no significant differences in the size, shape and color of MPs between groups. Conclusion: An increased MPs burden with the particular enrichment of PVC was observed in patients with AIT, suggesting a potential association between environmental MPs exposure and thyroid autoimmunity. Further mechanistic and epidemiological studies to clarify the impacts of chronic MPs exposure are needed. https://doi.org/10.1177/10507256261442506

Toxicité sur l'homme

Urinary non-persistent environmental chemicals in pregnancy: Associations with subclinical renal injury and exposure determinants,
Chen, C. C., Wang, Y. H., Wu, C. F., Hsieh, C. J., Wang, S. L., Chen, M. L., Tsai, H. J., Li, S. S., Cheng, C. M. and Wu, M. T., *Journal of Hazardous Materials Advances*, May 2026, Vol. 22.

Exposure to xenoestrogens-including phthalates, parabens, and phenols-as well as melamine is widespread; however, evidence regarding their combined effects on early renal injury during pregnancy remains limited. We examined associations between urinary concentrations of nine phthalate metabolites, four parabens, two phenols, and melamine and renal injury biomarkers-N-acetyl-beta-D-glucosaminidase (NAG) and albumin-tocreatinine ratio (ACR)-among 1433 pregnant women in Taiwan. Exposure determinants were assessed using structured questionnaires. Individual and cumulative exposure effects were evaluated by using compound-based summed exposure indices and principal component analysis (PCA) to characterize mixture patterns. In singlechemical models, methylparaben, butylparaben, nonylphenol, and bisphenol A were significantly associated with log-transformed NAG and ACR, while melamine was associated with NAG. Compound-based analyses revealed that phenols exhibited the strongest cumulative associations with both renal biomarkers, followed by parabens for NAG. Although individual phthalate metabolites were not significantly associated with renal markers, cumulative phthalate exposure was positively associated with ACR after covariate-adjusted creatinine standardization. PCA identified exposure patterns linked to personal care product use (parabens) and indoor environmental factors (phthalates), with regional variability observed. Phenols showed consistent associations despite uncertainty regarding dominant exposure sources. The stronger effects identified through compoundbased and PCA-derived mixture approaches underscore the importance of evaluating hazardous environmental contaminants as complex exposure profiles rather than as single chemicals. Given the heightened physiological susceptibility during pregnancy, these findings support mixture-oriented risk assessment and targeted exposure mitigation strategies to protect maternal renal health. https://doi.org/10.1016/j.hazadv.2026.101153

Endocrine-disrupting properties of heavy metal exposure contribute to the intergenerational effects on learning and memory,
Dias, G. R. M., Zomer, H. D., Silva, N. F. and Graceli, J. B., *Frontiers in Endocrinology*, Mar 26 2026, Vol. 17.

Heavy metals are increasingly recognized as endocrine-disrupting chemicals (EDCs) capable of perturbing neurodevelopment and cognition across multiple generations. Among these, methylmercury (MeHg), lead (Pb), and cadmium (Cd) remain global public health concerns due to their environmental persistence, bioaccumulation in food and water sources, and widespread human exposure. Evidence from epidemiological and experimental studies demonstrates that these metals

can interfere with hormonal signaling, neurogenesis, synaptic organization, neuroendocrine regulation and epigenetic programming-processes that are essential for learning and memory formation during critical developmental windows. Collectively, current evidence supports the view that MeHg, Pb, and Cd exposure act as potent neuroendocrine disruptors capable of producing intergenerational consequences on learning and memory. In this review, we highlight the recent findings of the effects of prenatal exposure to the three heavy metals (i.e., MeHg, Pg and Cd) on developing learning and memory. https://doi.org/10.3389/fendo.2026.1761556

Integrative computational and experimental analysis identifies MEK-mediated carcinogenic effects of bisphenol A and diethyl phthalate in head and neck cancer,
Ding, R., Quan, T. Q., Wu, J. X., Huang, R., Liang, L. D., Quan, Q. and Long, Z. Q., *Ecotoxicology and Environmental Safety*, Mar 1 2026, Vol. 312.

We investigated the carcinogenic effects of four endocrine-disrupting chemicals-bisphenol A (BPA), diethyl phthalate (DEP), dimethyl phthalate (DMP), and dioctyl phthalate (DOP)-in nasopharyngeal carcinoma (NPC) and thyroid carcinoma (THCA) using an integrated toxicogenomic-machine learning-docking-experimental pipeline. Intersection analysis identified 31 NPC-related overlapping genes and 39 THCA-related overlapping genes, with 19 shared core targets across both malignancies. These shared targets were enriched in oncogenic signaling pathways including Mitogen-activated protein kinase (MAPK), Phosphoinositide 3-Kinase-Protein Kinase B (PI3K-AKT), and Janus kinase/signal transducers and activators of transcription (JAK/STAT). A multi-algorithm machine learning framework constructed 113 predictive models and prioritized six diagnostic genes (CCNA2, CDK2, MET, F2, TYMS, PPARG). High expression of CCNA2 (HR=1.43, p = 0.016), CDK2 (HR=1.66, p = 0.002), MET (HR=1.58, p = 0.002), and PPARG (HR=1.45, p = 0.0072) was associated with worse overall survival, whereas TYMS and F2 were not significant. Molecular docking showed stable ligand-protein binding with energies from -5.2 to -8.1 kcal.mol-1, with the strongest affinities observed for BPA-CDK2 (-8.1) and BPA-PPARG (-8.1); DEP also showed strong binding to CDK2 (-7.0). In vitro, BPA and DEP (but not DMP/DOP) increased colony formation (p < 0.01), accelerated wound closure, upregulated oncogenic genes (e.g., CDK2/MET/CCNA2; p < 0.05), and elevated p-MEK without changing total MEK in 5-8 F and TPC-1 cells. Collectively, BPA and DEP promote head and neck tumor progression through MEK pathway activation and cell-cycle dysregulation. https://doi.org/10.1016/j.ecoenv.2026.119924

The contribution of phenolic endocrine-disrupting chemicals to breast cancer risk: A comprehensive bioinformatics analysis,
Dou, Y. H., Li, X. X., Li, M., Shang, J. and Xu, T., *Scientific Reports*, Feb 11 2026, Vol. 16, no. 1.

Bisphenol A (BPA), nonylphenol (NP), and octylphenol (OP) are common environmental phenolic endocrine disruptors and widely used industrial chemicals that have garnered significant attention due to their potential to disrupt endocrine functions. These compounds are known to interfere with hormonal activities, particularly those related to estrogen, and are linked to the onset and progression of breast cancer. This study aims to systematically investigate the potential relationship between BPA, NP, and OP and breast cancer risk, along with their underlying molecular mechanisms, by synthesizing data from multiple databases. We initially acquired the chemical structures and SMILES representations of BPA, NP, and OP from the PubChem database. Subsequently, we utilized multiple databases, including the Comparative Toxicogenomics Database (CTD), SEA, and Swiss Target Prediction, t0 estimate their probable biological targets. The predicted targets were standardized and consolidated to form a comprehensive target database. Breast cancer-related targets were subsequently identified from the GeneCards and DisGeNET databases, and their overlap with the targets of BPA, NP, and OP was analyzed to pinpoint potential breast cancer risk targets. To elucidate the functional pathways involved, we conducted Gene Ontology (GO) and Kyoto Encyclopedia of

Genes and Genomes (KEGG) enrichment analyses using the DAVID database. This analysis offered insights into the molecular pathways influenced by BPA, NP, and OP in the context of breast cancer. Additionally, we utilized machine learning algorithms, specifically Least Absolute Shrinkage and Selection Operator (LASSO) regression and Support Vector Machine (SVM), to identify nuclear targets linked to BPA, NP, and OP-induced breast cancer. These nuclear targets were further validated through differential expression analysis and Receiver Operating Characteristic (ROC) curve analysis using the GEO dataset GSE42568. We also performed a Single Gene Gene Set Enrichment Analysis (GSEA) to investigate the potential regulatory mechanisms of these nuclear genes in breast cancer. The infiltration of immune cells in breast cancer tissues was analyzed using single-sample gene set enrichment analysis (ssGSEA), and the correlation between nuclear targets and immune cell infiltration was examined. Finally, molecular docking and molecular dynamics simulations were conducted to assess the binding affinity and stability of BPA, NP, and OP with their nuclear targets. In this study, we integrated network toxicology, machine learning and multi-omics validation, and identified for the first time that BPA, NP and OP may induce breast cancer through 156 common targets; among them, MAOA, MGLL, ADRA2A, RPN2, GF1R and CTSD were identified as the key causative genes, with a diagnostic efficacy of 0.80-0.94 AUC. Mechanistically, these genes are concentrated in the GPCR/MAPK/JNK, sphingolipid, and prolactin signaling pathways, which regulate the Wnt/TGF-beta/chemokine network and dramatically modify the immunological infiltration of nine classes of M0-M2 macrophages and CD4(+) T cells. Molecular docking and kinetic simulations suggested the strong affinity of BPA for MGLL, and the complex was stabilized with >= 3 hydrogen bonds. In conclusion, phenolic endocrine disruptors may cause breast cancer through the "multi-target-immune microenvironment-metabolic reprogramming" axis, and MAOA, MGLL, ADRA2A, and RPN2 may serve as new targets for early detection and management. https://doi.org/10.1038/s41598-026-39706-x

Impact of PFAS exposure on lipid metabolic pathways: mechanisms and implicatins in carcinogenesis,
Ferguson, E. J., Tessmann, J. W. and Zaytseva, Y. Y., *Frontiers in Toxicology*, Mar 11 2026, Vol. 8.

Per- and polyfluoroalkyl substances (PFAS) are a large class of synthetic chemicals widely used in industrial and consumer products owing to their unique surfactant properties. Their environmental persistence and bioaccumulative nature have resulted in widespread contamination of water, soil, and food sources, raising significant concerns for human health. Epidemiological and toxicological studies increasingly associate PFAS exposure with elevated risks of cancers, including liver, kidney, breast, and testicular cancers; however, the mechanisms underlying these associations remain incompletely understood. One emerging explanation is that PFAS disrupt lipid metabolism, a pathway frequently reprogrammed during cancer initiation and progression. PFAS share structural similarities with endogenous fatty acids and can bind to lipid transport proteins and/or activate lipid-sensitive nuclear receptors. Current evidence indicates that PFAS exposure is associated with increased blood lipid levels, as well as dysregulation of key transcription factors-such as peroxisome proliferator-activated receptors and sterol regulatory element-binding proteins-that can link PFAS exposure to tumor-promoting metabolic alterations. These disruptions can impair dietary fatty acid uptake and de novo lipid synthesis, leading to abnormal lipid accumulation, oxidative stress, and activation of pro-oncogenic signaling pathways. The purpose of this review is to synthesize current evidence on how PFAS exposure contributes to carcinogenesis through the disruption of lipid metabolism. By integrating findings from population studies, mechanistic research, and molecular insights, this review highlights lipid dysregulation as a critical connection between PFAS exposure and cancer biology and underscores the need for deeper investigation into this pathway. https://doi.org/10.3389/ftox.2026.1768277

Exposure to per- and polyfluoroalkyl substances (PFAS) and development of autoimmunity in humans and animals: a scoping review,
Holm-Larsen, C. E., Siggaard, L. W. L., Sander, S. D., Ostengaard, L. and Husby, S., *Archives of Toxicology*, 2026.

PFAS are a group of persistent organic pollutants, that bioaccumulate and are associated with negative health effects. Reviews have suggested that the most critical effects of PFAS are on the immune system, but little is known of effects on development of autoimmunity. Our objective was to map and summarize available evidence concerning exposure to any PFAS and development/presence of autoimmunity, in humans and animals. We assessed studies reporting potential associations between PFAS exposure and autoimmune disease and/or autoantibodies. We searched MEDLINE, Embase, CENTRAL, Scopus, and Web of Science (02.15.2024) and conducted complimentary searches. Results were presented descriptively and we categorized autoimmune diseases and autoantibodies into relevant outcome groups. 51 studies were included, distributed in the following groups: Autoimmune thyroid disease, inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, type 1 diabetes, celiac disease, other diseases and autoantibodies. Cross-sectional studies were most common, limiting opportunities for causal inference. 33 studies showed associations between higher PFAS and increased risk of autoimmunity, while nine studies found lower PFAS associated with increased autoimmunity risk. The results suggest that PFAS have negative health impacts with strongest evidence for celiac and inflammatory bowel disease, weaker evidence for rheumatoid arthritis, systemic lupus erythematosus and type 1 diabetes mellitus. No clear indications of association with autoimmune thyroid disease. The majority of the studies showed an association between PFAS and autoimmunity. There is a need for more longitudinal and dose-response studies, to improve our understanding of individual autoimmunity outcomes in the future. Protocol registration: OSF.io (https://doi.org/10.17605/OSF.IO/3FEVQ). https://doi.org/10.1007/s00204-026-04381-4

Benzalkonium chloride and its derivatives as 5α-reductase 1 inhibitors to disrupt neurosteroid biosynthesis,
Huang, Y., Ding, C., Wang, S., Qi, S., Zhu, H., Wang, Y., Ge, R.-S., Liu, Y. and Cheng, J., *Bioorganic Chemistry*, 2026/07/15/ 2026, Vol. 176, p. 109850.

Biocide disinfectants are essential chemicals in infection control, but their use may cause adverse effects by inhibiting neurosteroid biosynthesis. In the current study we systematically examine the inhibitory effect of the biocide benzalkonium chloride (BAC), which is widely used for surface disinfection and as preservative in many consumer products, on human and rat 5α-reductase 1 (5α-R1) activity. The effects of BAC component (C1-C18) on brain 5α-R1 were investigated using HPLC-MS/MS measurement of steroid substrate testosterone and product dihydrotestosterone for enzyme inhibition screening assay and kinetics analysis, surface plasmon resonance (SPR) binding, intact cells, in silico docking and molecular dynamic simulations as well as structure-activity relationship (SAR)/3D-QSAR modeling. BAC component inhibited both human and rat 5α-R1, depending on alkyl chain length, with C10+ components exhibiting significant activity. C18 component emerged as the most potent inhibitor (IC_{50} = 9.54 μM for human 5α-R1; 34.36 μM for rat 5α-R1). SPR assay showed that C18 had a high affinity binding with KD of 6.42 μM with a relatively slow dissociation rate, indicating stable target engagement once bound. Mechanistic studies identified mixed/noncompetitive inhibition of 5α-R1 by BAC components by competing with NADPH (SPR assay). In intact SF126 cells, C12-C18 components suppressed 5α-dihydrotestosterone formation at 10-100 μM. Pearson correlation analysis linked inhibitory strength to structural parameters (LogP, molecular weight, alkyl carbon count, heavy atoms, and rotatable bonds). A 3D-QSAR pharmacophore model highlighted hydrophobic interactions as critical for inhibition. Molecular docking further

elucidated binding mechanisms, showing that BAC components occupy the NADPH-binding site via van der Waals forces, hydrogen bonds, hydrophobic contacts, and charge interactions. Our results suggest that BAC components have the potential to inhibit human and rat 5α-R1 activity and cause the neural disorders. These findings underscore BAC as potential endocrine disruptor by targeting neurosteroid biosynthesis, warranting further investigation into their neurotoxicological implications. This work was funded by the Zhejiang Nature and Science Foundation. The funders had no role in study design, interpretation or decision to publish. https://doi.org/10.1016/j.bioorg.2026.109850

Unraveling the endocrine disruption potential of microplastics in testosterone regulation,
Khawar, M. B., Afzal, A., Jalil, K., Jan, T. Y. Y., Ahmad, Z., Rehman, A., Afzal, H., Ahmad, S., Nimra, A. and Ashraf, M. A., *Journal of Environmental Sciences*, Jun 2026, Vol. 164, p. 827-836.

Microplastics (MPs) are increasingly recognized as emerging endocrine disrupting chemicals with significant implications for male reproductive health. Despite of well documentation on widespread presence in the environment, their specific effects on testosterone synthesis in humans remain insufficiently characterized. Current in vivo studies demonstrate that MPs impair androgen regulation through several interconnected mechanisms. These include oxidative stress-induced damage to Leydig cells, downregulation of antioxidant enzymes such as GPX1, disruption of the LH/cAMP/PKA/StAR signaling cascade essential for steroidogenesis, activation of NF-KB and inflammatory pathways, and induction of endoplasmic reticulum stress that accelerates testosterone metabolism. Additionally, MPs and their chemical additives interfere with steroidogenic enzymes and hormone receptors. Our review consolidates mechanistic insights linking MPs to testosterone disruption, underscores the dose-dependent nature of these effects. We also highlight critical knowledge gaps particularly the paucity of human data, the physicochemical diversity of MPs, and the long-term reversibility of endocrine disruption. https://doi.org/10.1016/j.jes.2025.12.063

Overloaded mitochondrial stress drives reproductive damage in GC-1 mouse spermatogonia cells exposed to nickel nanoparticle,
Kong, L., Liang, G. Y. and Wang, Y., *Cell Biology and Toxicology*, Feb 11 2026, Vol. 42, no. 1.

Nickel nanoparticles (Ni NPs) are widely used in industrial and commercial sectors, raising concerns about their potential occupational and environmental toxicity. Male infertility has increased significantly in recent decades, with environmental exposures playing a recognized role. Ni NPs have been identified as toxic agents that induce testicular damage and sperm abnormalities, yet their underlying molecular mechanisms are unknown. In this study, mouse spermatogonia GC-1 cells were used as an in vitro model to explore the role of mitochondrial autophagy (mitophagy) in the induced apoptosis of Ni NPs. Ni NPs significantly reduced cell viability, increased intracellular ROS levels, disrupted mitochondrial membrane potential, and triggered germ cell apoptosis. PINK1 and Parkin, key mitophagy-related proteins, exhibited significant upregulation. Cyclosporin A was used to inhibit mitophagy, attenuating mitochondrial damage and reducing apoptosis. In addition, PINK1 knockdown achieved by lentiviral transfection confirmed its critical role in mediating Ni NPs-induced mitophagy and subsequent cell death. These findings demonstrate that overactivation of the PINK1/Parkin pathway promotes apoptosis to Ni NPs exposure by mitophagy. Our study provides new mechanistic insights into the role of mitophagy in reproductive damage caused by nanomaterials. Graphical AbstractNickel nanoparticles induce mitochondrial dysfunction, oxidative stress, and apoptosis in GC-1 spermatogonia. Ni NPs activate excessive mitophagy through upregulation of the PINK1/Parkin pathway. Mitophagy inhibition by cyclosporin A alleviates mitochondrial damage and reduces apoptosis. PINK1 knockdown confirms mitophagy as a key driver of Ni NPs-induced germ cell death. https://doi.org/10.1007/s10565-026-10153-8

An environmentally relevant phthalate mixture impairs ovulatory prostaglandin and progesterone receptor pathways in human granulosa cells in vitro,
Land, K. L., Xu, H., Akin, J. W. and Hannon, P. R., *Environment International*, Mar 2026, Vol. 209.

Ovulatory defects are the leading cause of female infertility. Widespread exposure to endocrine-disrupting chemicals, such as phthalates, may contribute to the high prevalence of failed ovulation among infertile women. Using primary ovarian granulosa cells obtained from women, we tested the hypothesis that exposure to an environmentally relevant mixture of phthalate metabolites (MPTmix) impairs essential mediators of the ovulatory process, including progesterone (P4), progesterone receptor (PGR), and prostaglandins (PGs). The composition of the MPTmix was derived from urinary phthalate levels in women. Ovarian granulosa cells, obtained from in vitro fertilization patients, were acclimated in culture to regain responsiveness to hCG (human chorionic gonadotropin, clinical luteinizing hormone analogue). Following acclimation, cells were treated for 0.5-36hr with media containing DMSO (dimethyl sulfoxide, vehicle control), +/- hCG (to initiate the ovulatory cascade), and +/- MPTmix (1-500 & micro;g/ml). Compared to hCG controls, treatment with hCG + MPTmix reduced active ovulatory PG levels by up to 77%, likely via decreased synthesis (lower PTGS2 and PTGES levels/activity), enhanced catabolism of PGE2 to PGF2 alpha (elevated AKR1C1 and AKR1C3 levels), and increased metabolism (elevated HPGD levels/activity). MPTmix exposure further impaired PG function by altering the levels of PG transporters (ABCC4 and SLCO2A1) and receptors (PTGER1-4 and PTGFR). These MPTmix-induced disruptions were accompanied by upstream defects in LH/hCG receptor signaling (cAMP/PKA, ERK1/2), P4 steroidogenesis, and PGR expression. Together, these findings demonstrate that exposure to phthalates impairs P4/PGR-driven PG production/function in human ovarian cells and advances our mechanistic understanding of how phthalate exposure may contribute to ovulatory dysfunction in women. https://doi.org/10.1016/j.envint.2026.110183

Glycolytic metabolic reprogramming and mitochondrial dysfunction: A novel mechanism underlying PAEs-promoted cartilage inflammatory phenotype,
Liu, L., Chen, Y. C., Lin, W. Y., Zheng, M., Yu, T. Q., Chen, R. Y., Yang, Y. R., Jiao, L. L., Ruan, Q. L. and Sun, J., *Ecotoxicology and Environmental Safety*, Mar 15 2026, Vol. 313.

Phthalate esters (PAEs), the most prevalent class of plasticizers, are widely acknowledged as environmental endocrine disruptors (EDCs) and have been linked to the pathogenesis of various diseases. However, their specific role and intrinsic mechanism in inducing cartilage damage in bone-related diseases remain unclear. This study aimed to clarify the correlation between PAEs and cartilage damage, and to explore their potential molecular mechanisms. The core pathological change of knee osteoarthritis (KOA) is the progressive degeneration of articular cartilage. Based on this, this study first systematically explored the association between PAEs and KOA using network toxicology combined with molecular docking technology, and screened out core regulatory molecules including MMP9, EGFR, IL-10, BCL2, and CASP3. Subsequently, verification experiments on core molecules showed that PAEs exposure could activate the CASP3 pathway to induce apoptosis of human chondrocytes and significantly promote the formation of the inflammatory phenotype of chondrocytes. To further reveal the underlying mechanism, we conducted proteomic analysis and cell experiments in human articular chondrocytes (HCs). The results showed that exposure to PAEs triggered reprogramming of glycolysis metabolism, inhibited oxidative phosphorylation, and damaged mitochondrial homeostasis. Collectively, this study provides a robust theoretical basis for understanding the inflammatory phenotypes and underlying mechanisms of chondrocyte damage driven by PAEs exposure, and further lays a foundation for the design of novel therapeutic interventions and the optimization of environmental toxicity assessment protocols targeting PAEs. https://doi.org/10.1016/j.ecoenv.2026.120027

Bisphenol A and breast cancer: Can mechanistic plausibility be reconciled with epidemiological inconsistency?,
Liu, Y., Cao, H. L., Zhang, S. Y., Li, Q. H., Wang, X., Ma, M. Y., Zhou, Y. and Han, B., *Iscience*, Apr 17 2026, Vol. 29, no. 4.

This review synthesizes current evidence on the relationship between exposure to the environmental chemical bisphenol A, or BPA, and breast cancer risk. While laboratory studies demonstrate that even low concentrations of BPA can biologically promote breast cancer development and progression by interfering with hormonal signaling, altering cellular epigenetic regulation, and remodeling the tumor microenvironment, findings from large-scale population studies remain inconsistent. We find that many epidemiological studies in adult populations have failed to establish a clear, significant association between BPA exposure and breast cancer risk. However, when investigations use more precise exposure assessment methods, such as measuring the biologically active form of BPA, or focus on exposures during critical life stages such as fetal development or puberty in genetically susceptible subgroups, a significantly increased risk is frequently observed. This suggests that BPA may not pose a uniform risk to all individuals; its impact appears to depend on the timing of exposure, individual genetic susceptibility, and coexposure with other environmental chemicals. Given the strength of the mechanistic evidence and concerns over the potential long-term health consequences of early-life exposure, we conclude that although current human epidemiological evidence is not fully consistent, prudent preventive measures to reduce population exposure to BPA, particularly during sensitive periods such as pregnancy and childhood, are warranted. Future research requires the establishment of longitudinal cohorts that track individuals from early life, utilizing more accurate exposure assessment methods, to ultimately clarify the role of BPA in breast cancer. https://doi.org/10.1016/j.isci.2026.115421

Persistent organic pollutants and prostate cancer: multiple mechanisms and comprehensive control strategies,
Lv, C. S., Cao, H. L., Li, S. X., Du, H., Yang, L. C., Wang, L. M., Liu, S. Y., Zhou, H. L. and Gao, J. L., *Frontiers in Cell and Developmental Biology*, Mar 11 2026, Vol. 14.

Persistent organic pollutants (POPs) are a class of chemical substances with environmental persistence, bioaccumulation, and high toxicity, which are widely present in the environment and food chains. Prostate cancer (PCa) is a highly prevalent malignant tumor in the male reproductive system, and the association between its incidence and POPs exposure has attracted increasing attention. This review systematically summarizes recent epidemiological and experimental research evidence, indicating that multiple POPs are associated with the incidence risk, invasive progression, and poor clinical outcomes of PCa. A comprehensive mechanism analysis framework is constructed to clarify that POPs are associated with the occurrence and development of Pca mainly through four synergistic biological pathways: as endocrine disruptors, they interfere with androgen and aryl hydrocarbon receptor signaling pathways; potentially inducing epigenetic reprogramming including DNA methylation, histone modification, and non-coding RNA expression; may contribute to abnormal reorganization of cellular energy metabolism, lipid, and amino acid metabolism; and being linked to oxidative stress, which may lead to damage to the antioxidant defense system and genomic instability. Based on the above understanding of the mechanisms, we further propose a comprehensive prevention and control strategy covering the entire chain, including multi-dimensional public health intervention measures from source emission reduction, transmission pathway interruption to protection of susceptible populations. Moreover, we integrate the POPs exposure assessment into the whole-process clinical management of PCa, including the practical pathways for prevention, diagnosis, treatment, and prognosis. This review not only deepens the understanding of the complex mechanisms through which POPs are associated with PCa, but also provides a crucial

theoretical basis for formulating evidence-based, precise prevention and treatment strategies. https://doi.org/10.3389/fcell.2026.1741752

Endocrine disruptors are contributing to type 2 diabetes mellitus,
Magnifico, S., Hinault-Boyer, C. and Chevalier, N., *Hormones-International Journal of Endocrinology and Metabolism*, 2026.

The global prevalence of type 2 diabetes mellitus (T2DM) is rising exponentially, with alarming projections from the International Diabetes Federation estimating 589 million affected individuals in 2024 and more than 850 million in 2050. This represents an economic burden of approximately & euro;1,015 billion worldwide. Traditional explanations such as sedentary lifestyle and overeating are insufficient to explain such a rapid expansion of the disease. Increasing attention has therefore turned toward the role of environmental endocrine disruptors (EDs), and, in particular, of persistent organic pollutants (POPs). EDs are natural or synthetic molecules capable of altering endocrine function by interfering with biochemical pathways. They are omnipresent in daily life and have for several decades been implicated in reproductive or thyroid disorders, various hormone-dependent cancers (breast, prostate, testicular and colon cancers) and metabolic complications such as obesity. To better understand their diabetogenic potential, numerous experimental studies have been conducted. In vitro findings showed that certain POPs increase insulin resistance in cultured adipocytes or myocytes. Bisphenol A, widely used in plastic manufacturing, induces an initial hypersecretion of insulin in pancreatic islets, followed by a later decrease in insulin sensitivity. In vivo animal studies similarly demonstrate strong diabetogenic effects. In humans, epidemiological and longitudinal studies have revealed direct associations between exposure to POPs (e.g., organochlorine pesticides, dioxins, and polychlorinated biphenyls) and the onset of metabolic syndrome or T2DM. These effects were first observed after acute environmental exposure, such as the Seveso disaster. More recent large-scale studies confirm higher circulating levels of EDs in people living with obesity and/or T2DM, strongly demonstrating that these compounds are independent risk factors for insulin resistance. Collectively, the evidence now supports a central role of EDs in the global rise of obesity and T2DM. Their contribution to the epidemic is no longer speculative but increasingly recognized as scientifically established. https://doi.org/10.1007/s42000-026-00779-y

Bisphenol a and polycystic ovary syndrome in reproductive-age women: mechanistic exploration via network toxicology and molecular docking,
Peng, C. S., Wang, C. X., Chen, J. and Chen, H., *Journal of Ovarian Research*, Feb 28 2026, Vol. 19, no. 1.

Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine and metabolic disorder affecting 6-20% of reproductive-age women worldwide, characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, often accompanied by insulin resistance and infertility. Emerging evidence suggests that environmental endocrine-disrupting chemicals, such as Bisphenol A (BPA), may contribute to PCOS pathogenesis. This study employs network toxicology and molecular docking to elucidate the mechanistic links between BPA exposure and PCOS. By integrating multi-database analyses, we identified 294 BPA-related targets and 67 shared targets with PCOS, including key genes (PPARG, HSP90AA1, IGF1R, and INSR) implicated in hormonal dysregulation, insulin resistance, and inflammation. Protein-protein interaction (PPI) networks and enrichment analyses revealed their involvement in critical pathways such as estrogen signaling, ovarian steroidogenesis, and PI3K-Akt signaling. Molecular docking confirmed stable binding between BPA and these targets, with IGF1R exhibiting the strongest affinity (- 8.0 kcal/mol). Validation using the GSE5090 dataset demonstrated significant upregulation of PPARG and HSP90AA1 in PCOS patients. Our findings suggest that BPA disrupts follicular development, exacerbates hyperandrogenism, and impairs metabolic homeostasis

through multi-target interactions, providing novel insights into the environmental etiology of PCOS and potential therapeutic strategies. https://doi.org/10.1186/s13048-026-02049-2

Dietary Microplastics Engage Gut Mechanosensory-Endocrine Signaling to Disrupt Bone Homeostasis,
Romero, A. S., Phatak, S., Patil, S., Dar, H. Y., Rivas, J. A., Oyebamiji, O. M., Maes, B. B., Goitom, S. S., Enriquez, C. M., Orozco, J., Coffman, C. N., Liu, R., In, J. G., Campen, M. J., Cook, K., Levenson, R., Gross, J. M., Leng, S., Cretara, A., Pacifici, R. and Castillo, E. F., *bioRxiv*, 2026/04/07/ 2026.

Abstrait Les microplastiques (MP) sont des contaminants environnementaux omniprésents et un composant émergent de l'alimentation humaine ^{1,2} , mais leurs effets physiologiques restent mal définis. Nous montrons ici que les MP sont détectables dans l'os humain minéralisé en l'absence d'iatrogénie et qu'ils altèrent la minéralisation des ostéoblastes de manière dépendante du donneur. À l'aide d'un modèle d'exposition alimentaire physiologiquement pertinent, nous démontrons que l'ingestion chronique de MP induit une perte osseuse chez la souris, dépendante du sexe et du régime alimentaire, affectant principalement l'architecture trabéculaire, en l'absence de pathologie intestinale ou d'élévation systémique des cytokines inflammatoires. En revanche, l'exposition aux MP stimule sélectivement la signalisation sérotoninergique d'origine intestinale, avec une augmentation de l'abondance et de l'activité des cellules entéroendocrines sans signe de reprogrammation de lignage. Le profilage transcriptomique de noyaux uniques du côlon permet de distinguer les cellules entérochromaffines et l'expression des cibles sérotoninergiques dans les compartiments neuronaux épithéliaux et entériques, révélant des adaptations mécanosensorielles discrètes sans activation inflammatoire. Ensemble, ces résultats impliquent l'ingestion de microplastiques comme contaminant alimentaire bioactif qui perturbe la communication intestinale et endocrinienne et compromet l'homéostasie osseuse, révélant une voie jusqu'alors inconnue reliant l'exposition aux plastiques environnementaux à la santé osseuse. https://doi.org/10.64898/2026.04.03.716216

Synergistic toxicity of endocrine disruptors and environmental toxicants under climate change,
Seo, J., Jeong, M. and Ham, J., *Molecular & Cellular Toxicology*, 2026.

BackgroundClimate change, including global warming, has caused rapid environmental shifts in diverse ecosystems. Furthermore, as environmental pollution and exposure to endocrine-disrupting chemicals (EDCs) have become increasingly severe, numerous recent studies have investigated the combined effects of these two factors on ecosystems.ObjectiveThis review synthesizes the current evidence regarding the synergistic toxicological interactions between climate change factors (temperature and salinity) and EDCs across diverse taxa, including aquatic organisms, amphibians, livestock, and humans.ResultsThermal and saline stressors fundamentally altered the toxicokinetics and toxicodynamics of EDCs. Salinity shifts disrupt osmoregulatory homeostasis in aquatic species and amphibians, thereby enhancing their chemical bioavailability and sensitivity. In livestock and humans, heat stress activates the hypothalamic pituitary adrenal (HPA) axis and impairs hypothalamic pituitary gonadal (HPG) signaling, triggering a synergistic cascade of neuroendocrine and metabolic dysfunction. These physiological shifts, coupled with enhanced dermal absorption and thermally induced changes in clearance rates, significantly amplify the lethality and developmental toxicity of EDCs.ConclusionThese findings suggest that EDCs could exhibit greater toxic effects than originally reported and predicted, owing to their synergistic effects with environmental factors associated with rapid climate change. In addition, traditional risk assessments do not adequately account for these multiple factors or incorporate integrative multi-stressor models, and mechanistic studies are needed to strengthen regulatory frameworks. https://doi.org/10.1007/s13273-026-00617-7

Structural Insights into the Interaction of Bisphenol F (BPF) and Bisphenol S (BPS) with Estrogen Receptors for Endocrine Safety Assessment,
Sheikh, I. A., Bhat, I. U., Zughaibi, T. A., Ghorab, M. A., Rehan, M., Almutairi, M. F., Beg, M. A., Tariq, Z. and Kadry, A. R. M., *Toxics*, Mar 17 2026, Vol. 14, no. 3.

Endocrine-disrupting chemicals (EDCs) perturb hormonal homeostasis, dysregulating multiple biological pathways and subsequently resulting in adverse health outcomes, including impaired reproductive function. Bisphenols represent an important subclass of EDCs with widespread use in polycarbonate plastics, thermal paper formulations, epoxy resins, and various everyday consumer products. Bisphenol A (BPA) was the first bisphenol to be synthesized, with extensive industrial applications. However, the concerns over its potential health risks, most notably reproductive dysfunction, prompted the development and introduction of several structurally related BPA analogues. That said, studies on the potential hormonal effects of these BPA analogues remain limited. Therefore, strengthening the evidence base on their reproductive safety evaluation remains an essential priority for ensuring their safe application, and this study contributes to that broader objective. The study aimed to explore the potential endocrine-disrupting activity of two commonly used BPA analogues, bisphenol F (BPF) and bisphenol S (BPS), on reproductive hormone signalling, contributing to ongoing safety assessment efforts. The molecular interactions of these analogues with the estrogen receptor-alpha (ER alpha) and estrogen receptor-beta (ER beta) were analyzed through structural binding characterization employing the induced fit docking (IFD) approach using the Schrodinger 2019 suite. The overall results revealed that the two indicated BPA analogues were placed successfully in the ligand-binding pockets of ER alpha and ER beta. Their binding pattern and molecular interactions showed certain similarities; however, they did not fully replicate the amino acid residue environment of the native ligands of ER alpha and ER beta, estradiol. Notably, the binding energy estimations revealed that BPF and BPS showed substantially lower values than those calculated for native ligands of ER alpha and ER beta. In summary, this study suggests that BPF and BPS exhibit lower predicted binding affinity toward ER alpha and ER beta under the applied molecular docking conditions. However, these computational findings do not establish receptor activation, endocrine potency, or safety outcomes, and the potential involvement of other reproductive signalling pathways warrants further investigation. https://doi.org/10.3390/toxics14030262

Effects of bisphenol A and bisphenol S on human fallopian tube contractions: An in vitro and in silico study,
Singh, R., Sharma, P., Agarwal, S., Modanwal, S., Paulraj, S. and Mahto, S. K., *Reproductive Toxicology*, May 2026, Vol. 142.

Bisphenol A (BPA), a widely used industrial compound, and its structural analogue Bisphenol S (BPS) are known to exert reproductive toxicity. However, their direct impact on human fallopian tube contractility remains unexplored. This study aimed to investigate the effects of BPA and BPS on spontaneous smooth muscle contractions of the human fallopian tube. Fallopian tube samples from the proliferative phase were used for in vitro contractility assays. The effects of BPA and BPS (1-20 µM) on maximum contractile strength (MCS), basal tone (BT), and contraction frequency (CF) were recorded and analyzed using ANOVA. Cytotoxicity of both compounds was assessed in MCF-7 cells using the MTT assay. Molecular docking examined BPA and BPS binding affinities to key receptors. Both BPA and BPS significantly reduced contractile activity in a concentration-dependent manner ($p < 0.001$), with BPA exhibiting a stronger inhibitory effect than BPS. MTT assays demonstrated a significant dose- and time-dependent decrease in cell viability for both compounds. Molecular docking indicated comparable binding affinities of BPA and BPS toward estrogen, progesterone, oxytocin, prostaglandin, and calcium channel receptors. BPA and BPS impair human

fallopian tube contractility and exhibit cytotoxicity. These findings highlight potential reproductive risks associated with exposure to bisphenol compounds and underscore the need for subsequent extensive studies. https://doi.org/10.1016/j.reprotox.2026.109211

Mechanisms of reproductive toxicity and endocrine disruption of bisphenols and per-and polyfluoroalkyl substances (PFAS): Implications for women's reproductive health,
Stone, A. M., Fung, G. H., Joseph, A., Biernat, M. M., Camp, O. G. and Abu-Soud, H. M., *Reproductive Toxicology*, Aug 2026, Vol. 143.

Bisphenols and per-and polyfluoroalkyl substances (PFAS) are ubiquitous environmental endocrine-disrupting chemicals with widespread human exposure and growing concern regarding their reproductive toxicity. This review integrates current experimental and epidemiologic evidence to evaluate the potential endocrine-disrupting mechanisms and reproductive toxicity of bisphenols, particularly bisphenol A (BPA), and PFAS on female reproductive health. Available data demonstrate that these chemicals disrupt key hormonal and cellular processes regulating female reproduction, including hypothalamic-pituitary-ovarian axis signaling, ovarian steroidogenesis and folliculogenesis, oocyte quality and maturation, uterine structure and function, and oxidative stress. Across in vitro and animal models, BPA and PFAS consistently induce hormonal dysregulation, oxidative stress, mitochondrial dysfunction, and epigenetic alterations that impair coordinated ovarian-uterine signaling. Importantly, these mechanistic findings align with epidemiologic studies reporting associations between BPA and PFAS exposure and increased risk of adverse reproductive outcomes, including endometriosis, polycystic ovary syndrome, diminished ovarian reserve, premature ovarian insufficiency, infertility, and adverse pregnancy outcomes. Collectively, this review underscores the relevance of environmental chemical exposure as a modifiable risk factor for female reproductive health and emphasizes the need for further integration of mechanistic and population-based research to inform exposure assessment, risk evaluation, and regulatory strategies to reduce exposure to endocrine-disrupting chemicals and protect female reproductive health. https://doi.org/10.1016/j.reprotox.2026.109239

Decoding tamoxifen on idiopathic pulmonary fibrosis: integrating network toxicology and multi-omics,
Sun, Y. H., Lu, Z. Y., Yu, W. Y., Huang, S. Q., Xie, Y. X., Yao, D., Wang, H. W., Wu, Q., Huang, X. Y. and Li, X. C., *International Journal of Surgery*, Feb 2026, Vol. 112, no. 2, p. 2696-2716.

Background:Idiopathic pulmonary fibrosis (IPF) is a fatal interstitial lung disease with limited therapeutic options. Tamoxifen, a breast cancer therapeutic agent, raises environmental concerns due to its persistence and bioaccumulation potential, but its role as an endocrine disruptor in IPF pathogenesis remains unclear. Materials and Methods:We integrated computational toxicity prediction (ProTox-3.0/ADMETlab-3.0), FDA Adverse Event Reporting System (FAERS) pharmacovigilance, and Mendelian randomization (MR) to establish causal tamoxifen-IPF links. Network toxicology identified shared targets, with protein-protein interactions network construction revealing seven hubgenes. Multi-omics validation included: transcriptomics (GSE110147/GSE53845) for hubgenes expression, immune infiltration and single-cell RNA (scRNA) sequencing (GSE159354) for cellular associations, and machine learning (least absolute shrinkage and selection operator/support vector machine-recursive feature elimination/random forest) for biomarker identification. Mechanistic studies involved miRNA expression data (GSE27430) to explore the upstream regulators of key genes, and molecular docking to validate drug targets. Finally, in vivo validation was performed in C57BL/6 mice administered intraperitoneal tamoxifen, with assessment of pulmonary inflammation and fibrosis using bronchoalveolar lavage fluid protein exudation, cell counts, lung wet/dry weight ratio, and Ashcroft score, along with evaluation of epidermal growth

factor receptor (EGFR)/phosphorylated EGFR (p-EGFR) and miRNA-432-3p expression.Results:Computational toxicity prediction revealed tamoxifen's high respiratory toxicity potential, corroborated by FAERS-reported lung fibrosis associations, and MR confirmed causal IPF risk. Network toxicology identified seven hubgenes functionally enriched in miRNA regulation, with multi-omics validation revealing a critical EGFR dysregulation pattern where transcriptional downregulation contrasted with post-translational hyperactivation evidenced by elevated p-EGFR in fibrotic lungs. Mechanistically, miR-432-3p was upregulated in IPF and confirmed to directly target EGFR, while molecular docking demonstrated tamoxifen's preferential binding to miR-432-3p over EGFR. This tamoxifen-miRNA-EGFR axis drove pulmonary fibrosis with concurrent p-EGFR and mmu-miR-432 elevation in vivo. Conclusion:Tamoxifen promotes IPF via miR-432-3p-mediated EGFR suppression, establishing it as a pulmonary toxicant. Integrated network toxicology identifies EGFR as a diagnostic biomarker, highlighting environmental and clinical risks of tamoxifen exposure. https://doi.org/10.1097/js9.0000000000003620

Insights to cellular and molecular impacts of micro/nanoplastics and their additives for carcinogenic risks,
Verma, S. K., Mishra, S., Simnani, F. Z., Sinha, A., Kaushik, A., Ghosh, A. and Mishra, Y. K., *Results in Chemistry*, Jul 5 2026, Vol. 26.

The widespread use of plastics in daily life has led to the pervasive accumulation of microplastics and nano-plastics (M/N-Ps) in the environment. Their improper disposal and non-biodegradability have raised significant biomedical and ecological concerns. Recent evidence indicates that M/N-P exposure may be associated with the development and progression of various carcinogenic effects leading to cancers. However, despite growing evidence of M/N-Ps bioaccumulation in human tissues, a unified mechanistic framework linking M/N-Ps exposure to direct tumor progression across multiple cancer types remains absent from the literature. This review provides a comprehensive exploration of the cellular and biomolecular interactions between M/N-Ps, their additives, and human cells, detailing their detrimental effects. It further elucidates the hypothesized role of M/N-P exposure in cancer progression by investigating its proposed link to specific cancer types, including brain, oral, colorectal, lung, leukemia, prostate, ovarian, gastric, pancreatic, and breast cancer. The mechanistic pathways discussed include oxidative stress, DNA damage, chronic inflammation, and dysregulated cell signaling. Critically, this review advances beyond cataloguing inflammatory and oxidative effects to synthesize the evidence linking M/N-Ps to mechanisms of tumor cell proliferation and invasion. Additionally, the review highlights future research perspectives, addressing the need for in-depth mechanistic studies, improved detection methods, and regulatory policies. The mechanistic synthesis presented here offers researchers, clinicians, and policymakers a structured framework for understanding M/N-P induced oncogenesis, addressing a critical research gap in translating environmental plastic exposure data into organ-specific cancer risk assessment and therapeutic strategy. https://doi.org/10.1016/j.rechem.2026.103297

Metals/Metalloids Profile in Seminal Plasma/Serum of Patients with Asthenozoospermia/Oligozoospermia: Correlation with Semen Quality,
Wang, Y., Zhao, S. Y., Liu, Y. N., Zhang, J. B., Cao, L. Q., Jiang, P. and Qiao, Y. Y., *Biological Trace Element Research*, 2026.

Environmental exposure to metals/metalloids is linked to altered semen quality, but its influence on asthenozoospermia or oligozoospermia risk is unclear. This study aimed to investigate, in infertile men without known occupational or high-level environmental exposures, the differences in the distribution of metals/metalloids between seminal plasma and serum in infer-tile men with normal-quality (NQS) versus poor-quality semen (PQS) at background (general environmental) exposure levels. This cross-

sectional study recruited 141 infertile men (48 NQS group, 93 PQS group) from the Department of Reproductive Medicine of Jining First People's Hospital. Inductively coupled plasma mass spectrometry (ICP-MS) was used to determine levels of 18 common metals/metalloids in seminal plasma and serum. We analyzed distribution patterns across semen quality groups and biological matrices to assess overall and reproductive organ-specific exposure levels. Spearman's rank correlation evaluated associations between metals/metalloids levels and conventional semen parameters and testosterone (T) levels across the NQS, asthenozoospermia, and oligozoospermia subgroups. Multivariate linear regression was conducted to evaluate the robustness of significant findings. Compared with the NQS reference group, serum levels of four metals/metalloids includ-ing zinc (Zn), selenium (Se), iron (Fe), lithium (Li), showed significant alterations in the PQS group. Correlation analysis revealed moderate associations between levels of multiple metals/metalloids within the same matrix. After adjustment for age, body mass index (BMI), and abstinence period, serum Zn positively correlated with progressive motility (PR) and total sperm motility in the oligozoospermia subgroup, and serum Se negatively correlated with sperm concentration in the NQS group. These findings suggest that specific serum metals, particularly Zn and Se, are associated with semen quality in infertile men, with Zn potentially supporting motility and Se possibly adversely affecting concentration. https://doi.org/10.1007/s12011-026-05045-1

The Endocrine Disrupting Compounds Bisphenol-A and α-Zeranol Mimic the Estrogen Transcriptional Program to Promote Proliferation and Stemness in Breast Cancer Cells,
Winz, C., Li, E., Xie, C., Lee, K. C., Boguszewski, K., Rohatagi, S., Hahn, R., Rancourt, R., Furmanski, P. and Suh, N., *Molecular Carcinogenesis*, 2026/05/03/ 2026.

Excessive activation of the estrogen receptor (ER) drives proliferation, progression, and the formation of breast cancer stem cells (CSCs) in ER-positive breast cancer. Estrogenic endocrine disrupting compounds (EDCs) found in plastics, water, and food are also able to bind to the ER. Thus, we hypothesized that estrogenic EDCs mimic estrogen (E2) in the pathogenesis of breast cancer by promoting their survival and proliferation. Three estrogenic EDCs routinely found in human biosamples were selected for analysis: bisphenol-A (BPA), diethyl-hexyl phthalate (DEHP), and alpha-zeranol (αZAL). We assessed proliferation, transcriptional reprogramming, and CSC formation in breast cancer cell lines. E2, BPA, and αZAL significantly increased cell proliferation in ER-positive, but not ER-negative cell lines. This was reversed after administration of the ER-antagonist, ICI 182,780. BPA and αZAL upregulated estrogen target genes (PGR, TFF1) and increased levels of cell-cycle protein. RNA sequencing analysis revealed that BPA and αZAL altered expression of genes related to cell division, DNA repair, and estrogen signaling, with a substantial transcriptional overlap between EDCs and estrogen treatments. Additionally, BPA and αZAL increased the proportion of CSCs, defined as the CD24low/CD44high expressing subpopulation. Overall, these data indicate that BPA and αZAL act as functional estrogen mimics in breast cancer cells, activating canonical estrogen signaling pathways and promoting stem-like characteristics. Notably, this study provides the first transcriptomic and stem-associated characterization of αZAL in ER-positive breast cancer cells, revealing a robust estrogenic mode of action. This work provides mechanistic insight into how environmental EDCs may influence ER-positive breast cancer biology. https://doi.org/10.1002/mc.70127

Endocrine Noise: Sex-Specific Disruption of Hypothalamic–Pituitary–Adrenal (HPA) Axis by Endocrine-Disrupting Chemicals,
Xega, V., Yang, M. H. and Liu, J.-L., *Sexes*, 2026/06// 2026, Vol. 7, no. 2, p. 22.

Environmental chemicals are rarely considered stressors in the way that psychological or physical stressors are. Yet many endocrine-disrupting chemicals (EDCs) interact with the body's core stress

response system. This review examines how EDCs alter hypothalamic–pituitary–adrenal (HPA) regulation and how biological sex influences those responses. Drawing on human epidemiological data and experimental models, we describe how EDC exposure affects cortisol dynamics, feedback sensitivity, and adrenal signaling, with a particular focus on sex-dependent outcomes. We propose the concept of endocrine noise to describe how low-dose, often mixed EDC exposures introduce persistent interference into hormone signaling without necessarily causing overt endocrine deficiency or excess. In this framework, EDCs act as chronic, low-grade stressors that reset the timing, feedback precision, and rhythmic organization of the HPA axis rather than as isolated reproductive toxicants. We argue that EDCs should be understood as chronic, context-dependent stress modifiers that reshape sex-specific "risk architectures" for affective, metabolic, and immune disorders. Recognizing sex-specific HPA architecture and endocrine noise has immediate implications for study design and regulation, including the need for sex-stratified analyses, circadian-sensitive sampling of cortisol, and risk assessments that consider how the same exposure can push female and male stress systems in divergent directions. https://doi.org/10.3390/sexes7020022

Reproductive toxicity mechanisms of PNMC: Evidence from mitochondrial dysfunction and hormone synthesis disruption in the KGN cells,
Xie, J. Y., Pan, Z. X., Du, Y. H., Li, K. X., Liu, Y. N., Weng, Q. and Zhang, H. L., *Reproductive Toxicology*, May 2026, Vol. 142.

3-methyl-4-nitrophenol (PNMC), a widespread environmental endocrine-disrupting compound derived from diesel particulate matter and degradation of fenitrothion, poses a potential risk to ovarian function. This study investigated the concentration-dependent effects of PNMC on mitochondrial homeostasis and steroidogenesis using the human ovarian granulosa KGN cell line. Cells were treated with PNMC across a wide range of concentration (1 nM to 1 mM) for 48 h and mitochondrial dynamics and functions as well as steroidogenesis were evaluated. Transcriptional and immunofluorescence analyses showed that 100 mu M PNMC treatment significantly upregulated the expression of mitochondrial dynamics-related genes (MFN1/2, OPA1 and DRP1), mitophagyrelated genes (PINK1 and PARK2) and antioxidant defense-related genes (SOD1/2 and GPX1). These changes were associated with increased mtDNA copy number, reduced intracellular ROS and increased mitochondrial membrane potential. By contrast, 1 mM PNMC treatment provoked overt mitochondrial toxicity, characterized by diminished mtDNA content, elevated mitochondrial ROS, loss of membrane potential and significant decrease in cell viability. These results indicated that PNMC significantly altered the expression of genes related to mitochondrial dynamics, antioxidant defense, and mitophagy. The expression of CYP19A1 shows significant upregulation at 100 & micro;M PNMC treatment, while the maximal response for other genes (CYP17A1, CYP11A1, HSD3B) is observed at 1 & micro;M PNMC treatment. Correspondingly, the levels of 17 beta-estradiol and progesterone increased in the culture medium at 100 & micro;M or 1 & micro;M PNMC treatment, respectively. Collectively, these findings reveal that PNMC-associated dysregulation of steroidogenic function is closely linked to concomitant alterations in mitochondrial activity, providing important mechanistic insights into its potential reproductive toxicity. https://doi.org/10.1016/j.reprotox.2026.109223

PFAS and adipokines: Decoding their roles in the risk of breast nodules and breast cancer,
Xu, M. Y., Zhu, X. Y., Liu, Y. Y., Liu, X. Z., Liu, W. L., Lin, B. H., Zheng, Y. Y., Liu, K., Feng, Y., Alhazmi, N., Ma, S. T., Chen, H., Bai, Y. S. and Wang, H. H., *Environmental Research*, Jun 1 2026, Vol. 298.

Per- and polyfluoroalkyl substances (PFAS), recognized as endocrine-disrupting chemicals (EDCs), have been implicated in breast cancer development. However, the specific PFAS compounds link to both benign breast nodules and breast cancer development remain unclear. The roles of adipokines in these relationships warrant further investigation. This case-control study included 127 patients with

benign breast nodules, 278 patients with breast cancer, and 166 healthy controls. Serum concentrations of 10 PFASs, three adipokines (adiponectin, leptin, and resistin), and leptin to adiponectin ratio (LAR) were measured. Quantile-based g-computation (QGcomp) was employed to identify key PFASs associated with both benign breast nodules and breast cancer, and the interactions and mediating effects involving adipokines were explored. PFAS mixture exposure was associated with an increased risks of breast cancer [OR (95% CI) = 1.13 (1.05, 1.22)], whereas no significant association was observed for benign breast nodules [OR (95% CI) = 1.02 (0.86, 1.21)]. Five PFASs (PFOA, PFECHS, 6:2Cl-PFESA, PFOS, and PFUnDA) were implicated as risk factors for benign breast nodules, whereas six (PFHpA, 8:2Cl-PFESA, PFUnDA, PFECHS, PFNA, and PFHxS) were identified as risk factors for breast cancer. Notably, PFUnDA and PFECHS were identified as potential shared risk factors for both conditions, exhibiting positive associations with leptin and LAR, and negative associations with adiponectin. The association between PFUnDA and breast cancer risk was significantly amplified with increased leptin levels and LAR (P-interaction = 0.029 and 0.028, respectively). However, no significant interaction or mediation effects involving adipokines were otherwise detected (P > 0.05). These preliminary findings suggest a link between PFAS exposure and benign breast nodules, and identify PFUnDA and PFECHS as potential risk factors shared by both benign and malignant breast lesions. Adipokines appear to contribute to the PFAS-breast cancer associations. Further confirmation through large prospective studies is required to substantiate these initial observations. https://doi.org/10.1016/j.envres.2026.124293

Effects of Zearalenone on the Kiss1/GPR54 System and Related Genes Expression in the Hypothalamus and Pituitary Gland of Weaned Gilts,
Yuan, Z., Zhou, M., Luan, Y., Kong, L., Yang, W. and Jiang, S., *Toxins*, 2026/05// 2026, Vol. 18, no. 5, p. 195.

Zearalenone (ZEA) is a potent estrogenic mycotoxin known to disrupt reproductive functions, but its precise central neuroendocrine mechanisms remain unclear. This study investigated the effects of ZEA on the hypothalamic-pituitary Kiss1/GPR54 signaling pathway in weaned gilts. A total of 32 gilts were randomly assigned to four dietary treatments contained with 0, 0.15, 1.5, or 3.0 mg/kg ZEA for a 32-day feeding trial. Histopathology, immunohistochemistry, and mRNA/protein expression analyses of GPR30, Kiss1, GPR54, GnRH, and GnRHR in the hypothalamus and pituitary gland were conducted. ZEA exposure induced significant histological damage in both tissues. In the hypothalamus, Kiss1, GPR54, GnRH, and GnRHR exhibited a non-linear response, increasing at moderate doses and decreasing at 3.0 mg/kg ZEA, whereas GPR30 expression was continuously upregulated. In the pituitary gland, GnRHR showed a similar non-linear pattern. Furthermore, high-dose ZEA down-regulated pituitary Kiss1 and GPR54 while up-regulating GnRH and GPR30 expressions. In conclusion, ZEA induces reproductive neuroendocrine toxicity through a complex, dose-dependent modulation of the Kiss1/GPR54 signaling axis. The persistent upregulation of GPR30 suggests it acts as a crucial mediator in disrupting this endocrine feedback loop within the hypothalamus and pituitary gland. https://doi.org/10.3390/toxins18050195

The impact of Di(2-ethylhexyl) phthalate on human organ development: mechanisms and clinical relevance review,
Zhao, X., Hua, L., Xiong, Y., Shi, F., Zhong, Y., Zhang, S., Yu, D. and Tian, C., *Frontiers in Public Health*, 2026/05/04/ 2026, Vol. 14.

Di(2-ethylhexyl) phthalate (DEHP) is a commonly used plasticizer that has raised significant concerns due to its strong endocrine-disrupting effects, which are closely associated with developmental toxicity. While previous reviews have explored DEHP's developmental toxicity, this study uniquely focuses on recent (past 10 years) advances in understanding the molecular mechanisms behind DEHP-

induced organ developmental disorders. It emphasizes key pathways involved in cellular proliferation, differentiation, and endocrine balance. Despite widespread human exposure to DEHP, translating preclinical findings to human health outcomes remains challenging due to variations in exposure levels, individual susceptibility, and limited clinical data. This review compiles the latest clinical research on DEHP-related developmental health risks, explicitly addressing these uncertainties and exposure-related factors. By combining new molecular insights with clinical relevance, this review offers a focused scientific basis for future research into DEHP's developmental toxicology, bridging the gap between preclinical mechanisms and real-world human exposure outcomes. https://doi.org/10.3389/fpubh.2026.1830552

Network toxicology & molecular docking: endocrine-disrupting chemicals induce prostate cancer-a system study,
Zhou, Y., Zhou, G. M., Zhang, Y. J., Deng, C. H., Li, Z. S. and Hu, X. D., *International Journal of Clinical and Experimental Pathology*, 2026 2026, Vol. 19, no. 3, p. 116-129.

Objective: To elucidate the molecular mechanisms by which endocrine-disrupting chemicals (EDCs) initiate and sustain prostate carcinogenesis, thereby establishing a mechanistic foundation for the early detection and targeted intervention of castration-resistant prostate cancer (CRPC). Materials and methods: A total of 402 transcriptomic profiles from public GEO cohorts were integrated. Differential expression analysis, weighted gene co-expression network analysis (WGCNA), and network toxicology were jointly applied to prioritize candidate targets. Subsequently, an explainable XGBoost-SHAP machine-learning framework was employed to distill the core gene signature. The interaction affinities between selected EDCs and the corresponding proteins were computationally validated by molecular docking, with binding free energy (Delta G) serving as the quantitative metric. Results: Five genes-NR3C1, CALM1, MET, STAT3 and CES1-were identified as robust diagnostic biomarkers across multiple independent cohorts (AUC > 0.90). All five exhibited high-affinity binding to representative EDCs (Delta G <-7 kcal mol-1). Conclusions: For the first time, a seamless "transcriptome-network toxicology-structural biology" causal chain was established. By integrating explainable artificial intelligence with structural biology, this study closes a critical knowledge gap in the systems-level mechanism linking EDC exposure to prostate cancer initiation and progression, and offers novel, actionable targets for risk stratification and precision prevention. https://doi.org/10.62347/pgnw5316

Endocrine-disrupting chemicals and polycystic ovary syndrome: A systems toxicology perspective on mechanistic pathways,
Zhu, X. J., Xu, W. T. and Lu, A. F., *Reproductive Toxicology*, May 2026, Vol. 142.

This review presents a novel conceptual framework-the Multi-Hit, Multi-Level Cascade Model-that systematically integrates evidence from systems toxicology, molecular endocrinology, and epidemiology. Our model posits that chronic exposure to real-world EDC mixtures initiates a cascade of events wherein cellular perturbations (oxidative stress and low-grade inflammation) are amplified within the uniquely vulnerable ovarian microenvironment. This cascade then escalates into a systemic, self-perpetuating metabolic-endocrine-inflammatory vicious cycle, ultimately manifesting as the diverse clinical phenotypes of PCOS. Within this model, we formally propose three novel, testable hypotheses: the PCOS-specific vulnerability hypothesis, the cumulative susceptibility window hypothesis, and the mixture-driven synergistic toxicity hypothesis. By integrating fragmented evidence into a cohesive narrative, this framework not only provides a mechanistic understanding of EDC-induced PCOS pathogenesis but also identifies critical knowledge gaps and charts a roadmap for future research and targeted prevention strategies. https://doi.org/10.1016/j.reprotox.2026.109233

Méthodes

New Method to Sample and Determine 4-AP in the Workplace Air,
Dobrzynska, E. and Kowalska, J., *Aerosol and Air Quality Research*, Mar 25 2026, Vol. 26, no. 4.

A significant number of workers in the pharmaceutical and chemical industries, hairdressers and photographers are exposed to 4-aminophenol in the work environment. Due to its harmful effects by inhalation and ingestion, the possibility of causing allergic skin reactions, genetic defects and possible endocrine disrupting effects, a limit for its inhalable fraction in the working environment has been set at 5 mg/m3 in Poland. It was therefore necessary to develop a new sampling method by passing 360 L of air at a flow rate of 2 l/min through a glass fibre filter placed in the inhalable fraction sampler. Different types of filters were tested to retain the inhalable fraction of 4-aminophenol, and solvents for its extraction from the filter. Finally, 4-aminophenol extracted from the filter with acetonitrile was analysed chromatographically. The method has good precision and accuracy and meets the requirements of European standard EN 482 for chemical agent determination procedures and it was pre-verified at a cosmetics manufacturing company. https://doi.org/10.1007/s44408-026-00107-4

Application of the click analytical chemistry index for the assessment of endocrine-disrupting chemicals in cosmetics and personal care products,
Fuente-Ballesteros, A., Jano, A., Custodio-Mendoza, J. A., Samanidou, V., Mansour, F. R., Ares, A. M. and Bernal, J., *Journal of Chromatography A*, 2026/07/05/ 2026, Vol. 1778, p. 466990.

Cosmetics and personal care products often contain parabens, phthalates, and bisphenols, compounds used as preservatives or plasticizers that may also migrate from packaging materials into the product. Their potential endocrine-disrupting effects have prompted stricter regulations and concentration limits. Given their occurrence and the complexity of cosmetic matrices, several extraction and chromatographic techniques have been developed to ensure reliable quantification. In this review, representative methods published from 2018 to 2025 focused on the determination of these compounds were evaluated using the click analytical chemistry index (CACI), a recently developed color-coded tool that integrates analytical performance, environmental impact, cost, and applicability within a single framework. CACI allows an objective and balanced comparison of analytical methods, emphasizing practicality and real-world feasibility. The obtained CACI scores ranged from 57 to 80, suggesting that the evaluated methodologies can be categorized as acceptable (50–75%) or highly practical (>75%). It is expected that the use of CACI will promote the development of more sustainable, practical, and user-oriented analytical strategies for the evaluation of chromatographic methods, not only for endocrine-disrupting chemicals in cosmetics and personal care products, but also for other substances of interest. https://doi.org/10.1016/j.chroma.2026.466990

Determining EDC exposure: direct analytical methods are essential for accurate analysis of human biospecimens,
Gerona, R., Sovereign, A., French, D., Gonzaga, M. J., Vom Saal, F. S. and Hunt, P., *Journal of the Endocrine Society*, May 2026, Vol. 10, no. 5.

Purpose Estimates of human exposure are a major component of chemical risk assessment. Studies of bisphenol A (BPA) have raised concern that exposure has been underestimated because the lack of standards for the measurement of the major BPA metabolites has necessitated the use of flawed analytical tools to indirectly estimate them. Because other endocrine-disrupting chemicals (EDCs) are measured using similar indirect methods, we evaluated the accuracy of indirect analysis for representatives from three different classes of non-persistent EDCs that undergo rapid phase II

metabolism: bisphenols, parabens, and phthalates.Methods A direct LC-MS/MS method that simultaneously measures bisphenol S (BPS), propyl paraben (PrP), and monobutyl phthalate (MBP), and their major metabolites in urine, was used to quantify these EDCs in sixty second-trimester human urine samples. The same samples were also analyzed with a widely used indirect method that requires enzymatic hydrolysis before estimating metabolite levels. Results Marked discrepancies were evident when maternal urine samples were analyzed by both direct and indirect methods. Indirect analysis underestimated levels of all three EDCs and BPA, with the magnitude of underestimation varying by analyte. Conclusion The accuracy of widely used "indirect" analytical methods that estimate metabolite levels in human urine is neither predictable nor consistent. Greater precision and accuracy is attained using authentic standards for metabolites. Given the importance of biomonitoring data in estimating human EDC exposure, analytical accuracy is critical. Availability of standards for both the parent compound and its major metabolites should be required before a chemical enters the marketplace. https://doi.org/10.1210/jendso/bvag076

Machine Learning Prediction of Transthyretin Binding for Thyroid Hormone Transport Disruption for Chemical Risk Assessment,
Hou, S. K., Ji, C., Reh, C. M. and Ruiz, P., *Toxics*, Mar 10 2026, Vol. 14, no. 3.

Endocrine-Disrupting Chemicals (EDCs) disrupt thyroid hormone (TH) synthesis, transport, metabolism, and action, thereby perturbing systemic endocrine homeostasis. Transthyretin (TTR) is a key TH transport protein that regulates circulating hormone distribution and tissue availability, particularly during critical developmental windows. Chemical interference with TTR-binding may alter TH bioavailability and represent a transport-mediated molecular initiating event within thyroid-axis perturbation. Despite widespread exposure, many thyroidal EDCs remain unidentified, and their health effects are difficult to assess due to multiple simultaneous exposures. To support endocrine hazard identification and chemical prioritization within risk assessment frameworks, we developed machine learning-based QSAR models during the Tox24 challenge, using a dataset of 1512 chemicals to predict TTR-binding affinity. Of these, 67% were used for training, 13% for testing, and 20% for validation. Molecular descriptors were selected by first removing highly correlated features and then ranking the remaining descriptors using mutual information regression. The leverage approach was applied to define the models' applicability domain (AD). Five machine learning algorithms, including gradient boosting regressor (GBR), Random Forest, Lasso Regression, Support Vector Machine (SVM), and regularized SVM models, were developed. The GBR model demonstrated the best overall performance. This model achieved an R2 of 0.89 on the training set, 0.58 on the test set, and 0.55 on the validation set. The molecular descriptor analysis highlights hydrophobicity, steric effects, branching, connectivity, and ionization/electronic effects as the mechanistic basis for TTR disruption and stabilization, providing structural insight into features associated with thyroid hormone displacement. The AD analysis indicated that 97.5% of the test set and 96.0% of the validation set fell within the reliable descriptor space. Importantly, these predictions extend beyond model benchmarking by informing weight-of-evidence evaluations of thyroid-axis perturbation and supporting the prioritization of chemicals for targeted testing within non-animal new approach methodologies. Overall, this work highlights the application of in silico approaches for screening EDCs, supporting the prioritization and identification of potentially harmful chemicals. https://doi.org/10.3390/toxics14030240

Development of an in vitro method for simultaneous evaluation of androgenic activity of chemicals and their metabolites using S9: Application in biocides,
Kim, N. Y., Kwon, Y. K., Yang, E., Lee, G. and Lee, H. Y., *Food and Chemical Toxicology*, Jul 2026, Vol. 213.

EDCs such as pesticides and biocides may enter the food supply and be ingested by humans. Once absorbed, these substances are metabolized in the liver and subsequently distributed systemically. However, conventional in vitro assays assess only parent compounds, failing to consider the biological activity of metabolites formed through hepatic metabolism. This study integrated the S9 fraction, an enzyme extract from the liver tissue, into the OECD TG 458 assay to analyze Phases I and II metabolic processes. We introduced the non-metabolizable compound STZ as a new positive control, set a 6 h metabolism based on BPA and bicalutamide metabolism, and established metabolic activity criteria using STZ variability. Using this improved method, we evaluated AR activity and metabolic changes of 57 biocides regulated in Korea. The parent and metabolite forms of all biocides were negative for AR agonist activity. In the AR antagonist assays, 24 parent compounds were positive, 7 lost activity after metabolism, and 17 retained activity. This study demonstrated that incorporating hepatic metabolism into in vitro assays can classify EDCs whose toxicity is reduced through metabolism from those that retain endocrinedisrupting potential. Therefore, this approach may improve the identification of EDCs that pose a greater risk to human health. https://doi.org/10.1016/j.fct.2026.116076

Screening of Estrogenic and Antiestrogenic Effects of Estradiol, Bisphenol A, and Fulvestrant Using 2D and 3D Breast Cancer Cell Systems With a Luciferase Reporter Gene Assay,
Monteleone, V., Barbaro, K., Elisa, I., Daniele, M., Bisegna, S., Mollari, M., Galli, F., Cittadini, M., Zepparoni, A., Caciolo, D., Sittinieri, S., Altigeri, A., Alimonti, C., Ciurli, G., Cimmino, A., Cortese, F., Sagrafoli, D., Villa, R., Zilli, R. and Scicluna, M., *Journal of Applied Toxicology*, 2026.

Endocrine-disrupting chemicals (EDCs) like bisphenol A (BPA) pose health risks by interfering with hormones. This study develops and utilizes in vitro 2D and 3D cell models to evaluate the estrogenic and antiestrogenic properties of compounds. Human breast cancer cell lines T47D and MCF7, stably transfected with a luciferase reporter gene (ERE-LUC), were first compared in 2D. Due to the significantly higher sensitivity and responsiveness observed in the T47D line during preliminary 2D screenings, this cell line was exclusively selected for the development of the 3D spheroid model. Cells were treated with 17 beta-estradiol (E2), BPA, and Fulvestrant (FUL) to assess cell viability and luciferase activity. In 2D models, T47D ERE-LUC cells showed higher responsiveness than MCF7 ERE-LUC, which failed to show significant luciferase induction with E2. In the 3D T47D model, cells exhibited significant and robust changes in luciferase activity in response to E2 and BPA, highlighting the enhanced fidelity of 3D cultures in replicating tissue conditions compared to their 2D counterparts. The study highlights the effectiveness of 3D models over 2D in evaluating estrogenic activity. Specifically, the 3D T47D ERE-LUC system serves as a superior, sensitive, and reliable platform for screening EDCs, offering benefits in cost, data speed, and reduced in vivo reliance. https://doi.org/10.1002/jat.70168

EDC Profiler: A High-Throughput Screening Server for Identifying Endocrine Disrupting Chemicals toward Multiple Nuclear Receptors,
Qiu, Y., Cui, S., Zhang, H., Huang, Y., Chen, X., Zhao, Y., Zhuang, S. and Jiang, G., *Environmental Science & Technology*, 2026/05/05/ 2026.

Endocrine disrupting chemicals (EDCs) are associated with various adverse health outcomes, thus necessitating high-throughput screening. However, current EDC screening models struggle to achieve high predictive performance and biological interpretability. Considering the predominant contribution of molecular interactions between EDCs and nuclear receptors (NRs) to molecular initiating events associated with adverse health outcomes, it is essential to integrate chemical-NRs interactions profiles into EDCs screening. Herein, we develop mechanism-driven models by integrating chemical-NRs interactions features of 372 434 chemicals with 16 NRs from large-scale molecular docking and

chemical structural features, enabling comprehensive molecular representation of binding potential and physicochemical properties. Multiple models are constructed using diverse algorithms (XGBoost, NGBoost, Random Forest, TabPFN, and graph convolutional network), with SHAP analysis identifying key features of endocrine disruption to link predictions to chemical-NRs interactions. The optimal models achieved impressive performance (AUC: 0.815-0.995) and wide applicability with external validation against published EDCs inventory. The models are implemented in an open-access web server named EDC Profiler (http://www.edcprofiler.cn/service/edcprofiler), featuring interactive input interfaces, batch processing capabilities, and intuitive result visualization. The platform facilitates efficient EDCs screening and promotes new approach methods (NAMs) development for EDCs health risk assessment. https://doi.org/10.1021/acs.est.5c18135

Agenda, actualité, politique

Derrière le scandale du cadmium, une surexposition globale aux contaminants chimiques,
Techniques de l'Ingénieur
Le 25 mars 2026, l'Anses a publié un rapport alertant sur la surexposition des Français au cadmium, un métal toxique et cancérigène particulièrement présent dans l'alimentation et dont le risque sanitaire est depuis longtemps sous-estimé. Malheureusement, le cadmium n'est pas le seul contaminant chimique auquel les populations sont surexposées : il y a aussi les autres métaux lourds, les résidus de pesticides, les PFAS, les microplastiques, les dérivés du pétrole ainsi qu'une multitude d'additifs. https://www.techniques-ingenieur.fr/actualite/articles/derriere-le-scandale-du-cadmium-une-surexposition-globale-aux-contaminants-chimiques-158450/

Lithium : mieux connaître les expositions pour maîtriser les risques sanitaires et environnementaux
Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail.
Essentiel à plusieurs secteurs d'activités, comme la fabrication des batteries de voitures ou des téléphones, le lithium voit ses usages croître rapidement. En 2020, l'Anses avait mis en évidence la toxicité du lithium pour la reproduction aux doses présentes dans les médicaments. Au terme de deux nouvelles expertises, l'Agence a montré les propriétés de perturbateur endocrinien du lithium et a constaté un manque de connaissance sur les niveaux d'exposition via l'environnement et les effets associés. Elle recommande des mesures pour collecter les informations nécessaires à la prévention des risques potentiels correspondants. https://www.anses.fr/fr/content/lithium-mieux-connaitre-les-expositions-pour-maitriser-les-risques-sanitaires-et

New online course: EDCs 101 - EHN.
HEEDS has created an online course on endocrine disrupting chemicals and we are looking for people to try it out.This course is designed to break down how endocrine disrupting chemicals work inside the body and the supporting evidence about how these chemicals change the way we think about health. *https://www.ehn.org/new-online-course-edcs-101*
https://environmental-health-sciences-2e3799.circle.so/c/ehs-training-program

SCCS Scientific advice on Butylated Hydroxyanisole (BHA) - Public Health.
European Commission
Conclusion of the opinion:
In light of technical and scientific progress, available scientific literature, relevant in silico tools and the SCCS' expert judgement and taking under consideration in particular the concerns related to potential endocrine disrupting properties, the SCCS is requested:

1.to identify and justify whether there are specific concerns regarding the use of BHA in cosmetic products;
Based on the risk assessment, the SCCS considers the use of BHA in leave-on and rinse off cosmetic products up to a concentration of 0.07% as safe.
2. to highlight if there is a potential risk for human health from the use of BHA in cosmetic products;
This SCCS Scientific Advice considered only dermal use and hence, is applicable for the use of BHA in dermally applied products, and not in oral care products or cosmetic products which may lead to exposure of the end-user's lungs by inhalation.
The SCCS mandate does not address environmental aspects. Therefore, this assessment has not covered the safety of BHA for the environment. https://health.ec.europa.eu/publications/sccs-scientific-advice-butylated-hydroxyanisole-bha_en

Webinar. Prenatal Exposure to OP Pesticides: Health outcomes & potential mechanisms. May 19, 2026. 3 pm US Eastern Time,
Collaborative for Health & Environment.
Organophosphates (OPs) are a common class of neurotoxic pesticides. Exposure at even low doses can disrupt healthy development, particularly during susceptible windows such as pregnancy. In this EDC Strategies Partnership/Young EDC Scientists Showcase (YESS) webinar, Haleigh Cavalier, MPH, PhD and Eleanor Medley, MPH will discuss potential health outcomes and biological pathways associated with OP exposure during this vulnerable window using data from the New York University Children's Health and Environment Study (NYU CHES), a NYC-based birth cohort. https://www.healthandenvironment.org/che-webinars/97145

Chloroéthane : proposition de classement comme toxique pour la reproduction et perturbateur endocrinien.,
ANSES (28 avril 2026),
Sur la base d'études montrant des atteintes à la fertilité et au développement, l'Anses propose de classer le chloroéthane comme toxique pour la reproduction et perturbateur endocrinien pour la santé humaine et l'environnement dans le cadre du règlement CLP (classification, étiquetage et emballage des produits). Le dossier scientifique est soumis à consultation publique sur le site de l'Agence européenne des produits chimiques (ECHA) jusqu'au 26 juin 2026. https://www.anses.fr/fr/content/chloroethane-proposition-de-classement-comme-toxique-pour-la-reproduction-et-perturbateur

ECHA's Socio-Economic Analysis Committee agrees its draft opinion on PFAS restriction proposal,
ECHA (11 mars 2026),
The European Chemicals Agency's Committee for Socio-Economic Analysis (SEAC) has agreed its draft opinion on the universal restriction proposal on all per- and polyfluoroalkyl substances (PFAS). The draft opinion will be published soon for a 60-day consultation.
Voir aussi : https://echa.europa.eu/-/echa-supports-pfas-restriction-with-targeted-derogations
https://echa.europa.eu/-/echa-s-socio-economic-analysis-committee-agrees-its-draft-opinion-on-pfas-restriction-proposal

Etendre le nombre de phtalates classés toxiques pour la reproduction et perturbateurs endocriniens dans le règlement CLP,
ANSES (2 mars 2026),
Les phtalates sont des substances utilisées comme plastifiant dans différents produits du quotidien. Treize phtalates à chaîne moyenne sont déjà interdits ou restreints au niveau européen en raison de leur classement, dans le cadre du règlement européen CLP, comme toxiques pour la reproduction et de leur identification comme perturbateur endocrinien dans le cadre du règlement REACH. Sur la base

de ses travaux d'expertise toxicologique, l'Anses propose de classer une quarantaine de phtalates à chaîne moyenne comme toxiques pour la reproduction et perturbateurs endocriniens pour la santé humaine et l'environnement. Ce classement préviendrait les substitutions regrettables entre phtalates susceptibles de présenter des effets similaires. Le dossier scientifique est soumis à une consultation publique jusqu'au 27 mars 2026 sur le site de l'Agence européenne des produits chimiques (ECHA). https://www.anses.fr/fr/content/etendre-le-nombre-de-phtalates-classes-toxiques-pour-la-reproduction-et-perturbateurs

Le fluor dans les dentifrices est-il dangereux pour la santé ?
60 Millions de Consommateurs, 2026/04/13
Le fluor est-il un perturbateur endocrinien, toxique pour la reproduction, comme les autorités de santé le prétendent ou l'indispensable allié dans la lutte contre les caries ? Entre l'Anses et les dentistes, le débat fait rage. https://www.60millions-mag.com/hygiene-beaute/article/polemiquefaut-il-proscrire-les-dentifrices-au-fluor-20260413/

Lithium : mieux connaître les expositions pour maîtriser les risques sanitaires et environnementaux,
ANSES (2026),
Essentiel à plusieurs secteurs d'activités, comme la fabrication des batteries de voitures ou des téléphones, le lithium voit ses usages croître rapidement. En 2020, l'Anses avait mis en évidence la toxicité du lithium pour la reproduction aux doses présentes dans les médicaments. Au terme de deux nouvelles expertises, l'Agence a montré les propriétés de perturbateur endocrinien du lithium et a constaté un manque de connaissance sur les niveaux d'exposition via l'environnement et les effets associés. Elle recommande des mesures pour collecter les informations nécessaires à la prévention des risques potentiels correspondants. https://www.anses.fr/fr/content/lithium-mieux-connaitre-les-expositions-pour-maitriser-les-risques-sanitaires-et

Perturbateurs endocriniens : le Gouvernement consulte sur ses priorités et son plan d'actions,
Actu-Environnement, 2026/04/13.
Le gouvernement a ouvert la consultation publique sur les priorités d'actions et son plan dans la lutte contre les perturbateurs endocriniens. Il se décline en 20 actions pour six thématiques. https://www.actu-environnement.com/ae/news/plan-actions-perturbateurs-endocriniens-priorites-consultation-publique-47833.php4

Perturbateurs endocriniens et médicaments : le mal est-il dans le remède ?
Le Moniteur des pharmacies (2026/04/30),
Omniprésentes dans notre environnement, ces substances qui perturbent le système endocrinien se retrouvent aussi dans certaines spécialités. Parmi eux, les parabènes et les phtalates, utilisés comme excipients, constituent une source d'exposition encore peu prise en compte., https://www.lemoniteurdespharmacies.fr/therapeutique/vigilances/perturbateurs-endocriniens-et-medicaments-le-mal-est-il-dans-le-remede

PFAS restriction: ECHA Committees' opinions and next steps,
ECHA (7 mai 2026),
Following the publication of the final opinion of the Committee for Risk Assessment (RAC) and the draft opinion of the Committee for Socio-Economic Analysis (SEAC) on the per- and polyfluoroalkyl substances (PFAS) restriction proposal on 26 March, we will host a webinar presenting the key elements of both opinions.
The webinar will explain the conclusions reached so far by the two committees, on the hazards, emissions and risks of PFAS, the risk reduction potential of the proposed restriction and the socio-

economic impacts, including the availability of alternatives and possible derogations. It will also outline the next steps in the REACH restriction process. This webinar will not cover the on-going consultation on the SEAC draft opinion, as this was already done in a previous webinar in October 2025. https://echa.europa.eu/-/pfas-2026-echa-committees-opinions

Podcast: How Do Endocrine Disruptors Impact Our Health? | Health Matters | NYP,
NewYork-Presbyterian, 2026/03/11.
An obstetrician gynecologist explores how certain chemicals interfere with our hormones, and what we can do about it. https://www.nyp.org/healthmatters/podcast-how-do-endocrine-disruptors-impact-our-health

Replay Webinaire : Development and real-life application of adverse outcome pathways for endocrine disruption,
ECHA (14 avril 2026),
This ECHA science seminar features Associate Professor Anna Beronius from Karolinska institute, Sweden together with Professor Terje Svingen and Senior Officer Marie Louise Holmer from Technical University of Denmark (DTU Food). Their presentations cover insights from the EFSA PAN and EU MERLON projects, highlighting ongoing advancements in AOP development and explorations of predictivity of non-animal methods within the field of endocrine disruptor assessment. https://echa.europa.eu/-/development-and-real-life-application-of-adverse-outcome-pathways-for-endocrine-disruption

Vidéo - Metabolic endocrine disruptors: Methods for the identification of metabolism disrupting chemicals *ECHA / Utrecht University* (28 avril 2026),
Des chercheurs de l'Université d'Utrecht présentent les dernières avancées scientifiques concernant les perturbateurs endocriniens métaboliques et les méthodes d'identification de ces substances chimiques en toxicologie réglementaire. Ils expliquent comment les perturbations métaboliques sont apparues comme une modalité endocrinienne distincte, liée à l'obésité, au diabète, aux maladies cardiovasculaires et à la stéatose hépatique non alcoolique. Ce séminaire s'appuie sur les résultats de recherches financées par l'UE, notamment par le cluster EURION, qui a développé de nouvelles approches pour identifier les perturbateurs endocriniens au-delà des voies métaboliques traditionnelles.
La présentation aborde les progrès réalisés en matière de développement, de pré-validation et de validation des méthodes, en particulier pour l'adipogenèse et les tests liés à l'adiposité, tels que les tests de transactivation du PPAR-γ et les modèles d'adipogenèse à base de cellules souches humaines. Les améliorations apportées par la microscopie automatisée et l'analyse multicritères sont discutées, ainsi que l'intégration des approches in vitro, in silico et de convergence des preuves. Les principaux défis liés à l'adoption réglementaire sont également abordés, notamment la validation des essais, la complexité des mécanismes et la variabilité des réponses biologiques. https://www.youtube.com/watch?v=aZ9xKRoj79E

Webinaire : Des micro et nanoplastiques aux PFAS : recherches sur ces pollutions diffuses. jeudi 28 mai. 11h/12h30.,
ANSES (28 mai 2026),
Série de 4 webinaires organisée à l'occasion des 20 ans du PNR EST dont l'objectif est de soutenir la communauté scientifique dans sa production de connaissances en santé environnement et santé travail. Au programme, la présentation de résultats de projets de recherche récents, financés par le PNR EST, et des travaux de l'Anses sur le thème des pollutions diffuses. Ce webinaire, animé par Matthieu Schuler, directeur général délégué du pôle Sciences pour l'expertise de l'Anses, permettra de discuter du lien entre la recherche et l'expertise et de leur utilité pour les politiques publiques.

Suivi des polluants microplastiques aux interfaces des milieux biologiques
Toxicité des micro et nanoparticules de plastiques vis à vis d'organismes aquatiques le long du continuum eau douce - eau marine : évaluation du transfert trophique
Analyse des résidus plastiques issus de la digestion humaine simulée de moules contaminées par des microplastiques, à l'aide du couplage entre la microscopie électronique à balayage et la spectroscopie Raman
Biomarqueurs associés à l'exposition aux PFAS : une approche transgénérationnelle
Travaux de l'Anses sur les PFAS : Bilan de la contamination et catégorisation en vue de leur surveillance
Discussions et échanges
https://ajspi.com/communiques-club/invitation-presse-4-webinaires-pour-feter-les-20-ans-du-pnr-est/
https://survey.anses.fr/SurveyServer/s/DFRV/polludiff/questionnaire.htm

Empowerment et rupture d'habitudes : une étude qualitative sur le changement de comportement vers des cosmétiques plus sains pour la santé,
Berenguel, G., Ojeda Trujillo, M.-B., Helme-Guizon, A., Louvel, S. and Philippat, C., (2026/05),
En 2024, le marché français de la beauté a atteint 22,8 milliards d'euros, selon Xerfi. 63% des Français ont déclaré dépenser entre 10 et 50€ par mois dans cette catégorie de produits (Opinion way pour Blissim, 2023). Or, par l'utilisation seule des produits de soin et cosmétiques, la population est ainsi exposée à plus de 160 substances chimiques par jour (Ficheux et al., 2019). Plusieurs de ces substances (e.g., paraben, phenols, phthalates etc.) sont suspectées d'être des perturbateurs endocriniens (Larsonn et al., 2014), nocives pour l'environnement et la santé en perturbant notre système hormonal (OMS). En effet, ces perturbateurs sont notamment responsables de l'augmentation de certains cancers (Schug et al., 2016), de troubles liés à la reproduction et la fertilité (Martin et al., 2022) ou encore des troubles de l'apprentissage et du comportement (Bergman et al., 2012). Au vu de ces risques, le Ministère de la Transition Ecologique et de la Cohésion du Territoire (2021), recommandent d'appliquer le principe de précaution et de limiter l'exposition. Toutefois, divers facteurs compliquent l'évitement de ces substances. En effet, les individus ne perçoivent pas le risque lié aux produits cosmétiques et les substances qui les intègre de façon équivalente (Bertin, 2023), les listes d'ingrédients peuvent être difficiles à lire (Okman et Yalçın, 2024), et les alternatives à ces substances sont parfois douteuses (Martin et al., 2022). Ainsi, la réduction de l'exposition dépend de la capacité des individus à comprendre des informations complexes et à agir en conséquence ; d'où l'importance de renforcer l'empowerment individuel, défini comme un processus psychologique permettant d'agir de manière autonome vers ses propres objectifs (Spreitzer, 1995 ; Zimmerman, 1995). Ce processus repose sur quatre dimensions — compétence, autonomie, sens et impact perçu — et peut évoluer ou être renforcé via des interventions, et changer au fil du temps (Zimmerman, 1995). Selon Verplanken et al. (2008), un changement de contexte qui perturbe les habitudes ouvre une fenêtre propice à une réflexion plus délibérée sur les comportements (ici de choix des produits de soin et cosmétiques). Nous étudions ainsi dans quelle mesure une intervention visant à rompre temporairement les habitudes (Habit Discontinuity Theory) peut renforcer l'empowerment. À notre connaissance, il s'agit de la première recherche reliant cette théorie aux quatre dimensions de Spreitzer pour analyser son impact potentiel sur l'empowerment. Cette recherche vise à répondre à quatre questions : dans quelle mesure la rupture des habitudes favorise-t-elle l'empowerment (Q1) ? Comment l'empowerment psychologique soutient-il les changements comportementaux positifs ou négatifs (Q2) ? Pourquoi certains individus évoluent-ils vers des changements positifs tandis que d'autres restent neutres ou abandonnent le changement (Q3) ? Et, à différents niveaux, comment maximiser cette « fenêtre de changement » (Q4) ? Les objectifs de l'étude sont ainsi d'évaluer les perceptions de risque liées aux perturbateurs endocriniens, d'observer les réponses comportementales et d'identifier les facteurs favorisant ou freinant le changement aux niveaux

individuel et collectif, à partir d'entretiens semi-directifs. Elle se situe ainsi à l'intersection de l'empowerment (Spreitzer, 1995 ; Zimmerman, 1995) et de la Habit Discontinuity Theory (Verplanken et al., 2008, 2018). https://hal.science/hal-05608096

Impacts of environmental stressors on fertility and fecundity across taxa, with implications for planetary health,
Brander, S. M., Swan, S. H., Mehinto, A. C., Kidd, K. A., Weis, J. S., Belcher, S. M., Dewitt, J. C., Harper, S. L. and Helbing, C. C., *npj Emerging Contaminants*, 2026/04/23/ 2026, Vol. 2, no. 1, p. 12.
Exposure to synthetic chemicals occurs across species. These substances are often untested, highly persistent, and lack regulation. Together with climate change, they can cause population decline. Many act as endocrine-disrupting chemicals, interfering with hormones at low concentrations. Emerging pollutants, including microplastics and per- and polyfluoroalkyl substances, further contribute. Impacts include reduced fertility, fecundity, and even multigenerational harm. Cross-species evidence underscores the need for systemic approaches to protect biodiversity and planetary health. https://doi.org/10.1038/s44454-026-00032-6

Réduire son usage des cosmétiques permet de diminuer rapidement l'exposition à certains polluants chimiques et perturbateurs endocriniens comme le bisphénol A,
Cara, G., *Salle de presse de l'Inserm* (2026/04/22),
Utiliser moins de produits cosmétiques et de soin peut réduire rapidement l'exposition à plusieurs substances chimiques incluant des perturbateurs endocriniens avérés ou suspectés, selon une étude publiée le 7 avril dans Environment International par des chercheurs de l'Inserm, de l'Université Grenoble Alpes et du CNRS, au sein de l'Institut pour l'avancée des biosciences et soutenue par la Commission européenne. Menée auprès d'une centaine d'étudiantes, elle montre que diminuer le nombre de produits cosmétiques et de soin utilisés et recourir à des alternatives exemptes de plusieurs composés suspectés d'être d'avoir des effets néfastes sur la santé (dont le méthylparabène et certains phtalates) s'accompagne d'une baisse des concentrations urinaires de ces substances en seulement cinq jours. Une diminution de la concentration du bisphénol A est également observée. Cette substance, classée par l'Union européenne comme « très préoccupante », est un perturbateur endocrinien et reprotoxique avéré, désormais interdit dans les cosmétiques.,
https://presse.inserm.fr/reduire-son-usage-des-cosmetiques-permet-de-reduire-rapidement-lexposition-a-certains-polluants-chimiques-et-perturbateurs-endocriniens-comme-le-bisphenol-a/72662/

Epidemiological studies and disease burden assessment of emerging contaminants,
Cui, Y. D., Xu, T. B., Niu, Y., Chen, R. J., Ji, J. S. and Kan, H. D., *Chinese Science Bulletin-Chinese*, 2026 2026, Vol. 71, no. 12, p. 2587-2601.
Emerging contaminants (ECs) are synthetic or naturally occurring chemical substances that are increasingly detected in the environment, posing potential health risks to humans. Due to their environmental persistence, bioaccumulation, and widespread exposure, ECs have become a pressing global public health threat. Specifically, these substances span diverse categories, including persistent organic pollutants (POPs), endocrine-disrupting chemicals (EDCs), antibiotics, and microplastics. Biomonitoring studies have shown that ECs are commonly detected in human biological matrices such as blood, urine, and adipose tissue, confirming ubiquitous internal exposure and underscoring the urgency for comprehensive risk assessment. A substantial body of epidemiological studies has identified associations between exposure to ECs and diverse adverse health outcomes. It has been shown that endocrine-disrupting chemicals, including per- and polyfluoroalkyl substances (PFAS), bisphenol A (BPA), and phthalates (PAEs), are closely linked to reproductive health issues. Such outcomes include reduced male semen quality, increased risks of female reproductive disorders such as polycystic ovary syndrome and endometriosis, and adverse pregnancy outcomes like preeclampsia

and impaired fetal development. Furthermore, ECs such as PFAS, PAEs, and antibiotics may disrupt the body's metabolic balance through endocrine disruption, lipid metabolism alterations, and other mechanisms, contributing to the rising prevalence of obesity, type 2 diabetes, and thyroid dysfunction. Additional evidence links various contaminants to thyroid, breast, and other cancers. The integrity of the cardiovascular, neurological, and respiratory systems is also at risk. Studies have linked ECs exposure to neurodevelopmental disorders, while the detection of micro- and nanoplastics in atherosclerotic plaques suggests their potential mechanistic involvement in cardiovascular disease. Moreover, numerous studies have focused on vulnerable populations such as infants, young children, and pregnant women, as exposure to environmental toxicants during critical developmental or physiological stages may lead to significant and lasting health effects. Despite the evidence, current research on the disease burden of ECs remains limited and faces significant methodological hurdles. Although ECs are confirmed to pose serious health threats, existing evidence and subsequent disease burden estimations, primarily based on biomarker-derived exposure levels, suffer from wide confidence intervals in effect estimates and, more critically, uncertainty in exposure-disease causality. Such uncertainty often stems from reliance on cross-sectional or case-control study designs that are inadequate to establish temporality. The assessment is further complicated by the unique toxicological properties of ECs, including non-monotonic dose-response relationships and low-dose effects, as well as the challenge of evaluating the synergistic effects of complex chemical mixtures. A critical limitation stems from regional disparities in data, highlighting the need for more comprehensive, multidimensional exposure assessments and cross-population validation. Findings from Western cohorts cannot be directly extrapolated to regions such as China, which has distinct exposure patterns and population susceptibilities. To address these profound gaps, this study proposes a comprehensive "mechanism analysis - assessment optimization- closed-loop governance" paradigm. This paradigm works by integrating insights from multidisciplinary approaches to build an innovative research framework. Mechanism analysis emphasizes the elucidation of complex biological pathways and the identification of early biomarkers, advocating for the deeper integration of multi-omics technologies to move beyond single-endpoint toxicology. Assessment optimization calls for the innovation of disease burden assessment methods, particularly through the adoption of advanced tools such as artificial intelligence to model high-dimensional data, non-linearities, and complex mixture effects. Furthermore, the paradigm promotes the translation of scientific evidence on ECs into policy through a closed-loop governance system incorporating national dynamic monitoring, the generation of high-quality local evidence, cost-benefit analysis of interventions, and a multi-stakeholder framework, thereby enhancing risk management and protecting public health in a targeted and effective manner. https://doi.org/10.1360/csb-2025-0225

ONE HEALTH SUMMIT : Santé-environnement : la France change d'échelle avec une stratégie nationale fondée sur “Une seule santé”,
Dgs_Céline.M and Dgs_Céline.M, *Ministère de la Santé, de la Famille, de l'Autonomie et des Personnes handicapées*.
Sous l'impulsion du Président de la République, la France organise à Lyon, du 5 au 7 avril 2026, le One Health Summit. Consacré à l'approche « Une seule santé », ce sommet vise à mieux prévenir les risques sanitaires en agissant à l’interface entre santé humaine, animale et environnementale. Dans un contexte d’intensification des risques et de fragmentation de l’action internationale, il réunit États, organisations internationales, scientifiques et acteurs économiques afin d’accélérer des réponses concrètes. Les travaux s’articulent autour de quatre priorités : maladies infectieuses, résistance aux antimicrobiens, systèmes alimentaires et pollutions. Dans ce cadre, la France annonce également des mesures nationales pour traduire cette approche dans ses politiques publiques. https://sante.gouv.fr/actualites-presse/presse/communiques-de-presse/article/one-health-summit-sante-environnement-la-france-change-d-echelle-avec-une

Cadmium : pourquoi les femmes sont plus exposées,
Hiver, L., *Vert* (2026/04/09),
Cadmium de force majeure. Omniprésent dans l'alimentation, le cadmium suscite l'inquiétude des autorités sanitaires. Ce métal lourd, notamment issu des engrais phosphatés, affecte particulièrement les femmes sujettes au manque de fer, avec des conséquences importantes sur leur santé., https://vert.eco/articles/cadmium-pourquoi-les-femmes-sont-plus-exposees

Réglementation européenne et actions administratives françaises face aux perturbateurs endocriniens : vers une harmonisation des critères d'identification pour une prise en compte efficace au niveau national,
Michel-Caillet, C., *Environnement, Risques & Santé*, 2026/03/01, Vol. 25, no. 2, p. 123-130.
https://doi.org/10.1684/ers.2026.1918

"If They Are Not Labeled, How Do We Know What's Risky and What's Not?": Assessing Information on Brominated Flame Retardants in Children's Plastic Products in South Africa,
Mlelwa, R. and Rother, H. A., *Environmental Health Insights*, 2026 Vol. 20.
Background: Global literature indicates that polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCDD), types of brominated flame retardants (BFRs), are increasingly found in children's plastic products. These products are widely sold in South Africa. PBDEs and HBCDD are persistent organic pollutants (POPs) banned under the Stockholm Convention due to their severe health impacts, including endocrine disruption, neurotoxicity, and cancer. Information about chemicals present in these plastic products is necessary to inform risk reduction measures. Methods: This study assessed the availability and accessibility of information on POP-BFRs in children's plastic products in South Africa to enhance stakeholders' capacity to implement risk reduction measures. The study was guided by the chemicals-in-products (CiP) information-sharing framework developed by the United Nations Environment Programme (UNEP) in 2015. Data collection involved in-depth interviews and an online survey. South African stakeholders participated, including those involved in manufacturing, regulation, and advocacy (n = 10) and consumers (n = 44). Data was analyzed thematically using NVivo.Results: CiP information on POP-BFRs in children's plastic products was largely unavailable. Regulatory and advocacy stakeholders had limited general information on POP-BFRs and the associated risks. Additionally, they had limited access to POP-BFRs information, while consumers had none. Conclusion: National and international coordinated actions are necessary to close the POP-BFRs information gaps. The South African government should develop and enforce an overarching chemical legislation, establish a national chemical register, and require full disclosure of CiP. UNEP should establish a global standardized system for CiP information under the 2023 Global Framework on Chemicals. https://doi.org/10.1177/11786302261435748

Projet de priorités d'actions de l'Etat et de plan d'actions sur les perturbateurs endocriniens,
Publiques, C., *Consultations publiques*, 2026/04/10.
La présente consultation concerne un projet de priorités d'actions de l'Etat et de plan d'actions sur les perturbateurs endocriniens (PE). https://www.consultations-publiques.developpement-durable.gouv.fr/projet-de-priorites-d-actions-de-l-etat-et-de-plan-a3335.html

Research priorities for the adverse health effects of emerging contaminants,
Tang, S., Lyu, Y. B., Wang, Q., Duan, L. N., Gu, W., Xu, Y. J., Yang, X. Y., Lu, Y. F., Shen, H. B. and Shi, X. M., *Chinese Science Bulletin-Chinese*, 2026 2026, Vol. 71, no. 12, p. 2571-2586.
Accelerated industrialization and urbanization have precipitated the global emergence of persistent, bioaccumulate, and toxic environmental contaminants-collectively termed emerging contaminants (ECs). These substances pose increasingly complex, transboundary, and systemic threats to public health. Therefore, they demand urgent, interdisciplinary, and innovation-driven interventions at the

science-policy interface. Against this backdrop, this review synthesizes current evidence on human-exposure patterns, multi-endpoint health effects, molecular toxicodynamics, and predictive risk frameworks for ECs, and critically examines knowledge gaps and methodological limitations in existing research. In the context of China, effective EC management is hindered by fragmented evidence of life-course health effects and inadequate health-oriented regulatory infrastructure. The rapidly evolving chemical landscape and insufficient integration of health data exacerbate these challenges. To address them, we propose an integrated research framework prioritizing the following four transformative domains. (1) Advanced exposure surveillance. Multi-media, high-resolution analytical platforms and nationwide spatiotemporal monitoring networks are needed to capture dynamic EC profiles across environmental matrices and biological samples. This requires overcoming bottlenecks in ultra-trace detection and non-targeted screening, and harmonizing multi-pathway exposure assessments, particularly for vulnerable populations and high-risk occupational cohorts. Leveraging next-generation exposure measurement technologies and realtime data analytics will enable adaptive, precise monitoring and provide early warnings for EC hotspots. Such networks will enhance our ability to track and predict the spread of ECs and allow for targeted interventions. (2) Holistic health impact assessment. A transition from reductionist, single-pollutant models to systems toxicology approaches is essential. Key priorities include constructing population-scale health-effect spectra and exposome-wide biomarker panels to comprehensively account for real-world mixture exposures. Leveraging functional exposomics, integrated with longitudinal cohort studies and multi-omics technologies, will elucidate critical life-course exposure windows and latent health risks. Integrating environmental, clinical, and socio-behavioral data will enable nuanced risk stratification and tailored public health responses. This comprehensive approach will be crucial for developing effective public health strategies. (3) Mechanistic toxicology innovation. New approach methodologies (NAMs) integrating organoids, CRISPR screening, multi-omics, and computational biology can be used to explore non-monotonic dose responses, identify novel toxicity pathways, and decipher mixture interactions. Establishing a robust, open-access localized toxicological database is essential to support next-generation risk assessment and adverse outcome pathway development. Synergizing in vitro, in vivo, and in silico models will accelerate mechanism-based discovery and translational application to improve understanding of the mechanisms underlying EC effects on human health for more precise interventions. (4) Intelligent risk forecasting. Implementing artificial intelligence (AI)-driven predictive frameworks that assimilate multi-omics data streams, environmental monitoring datasets, and population health records through deep-learning architectures will facilitate real-time risk stratification, early intervention, and the development of dynamic health-based guidance values. Concurrently, quantification of EC-attributable disease burdens and intervention benefits is vital to inform evidence-based policy. AI-driven approaches can enhance the speed and accuracy of risk assessments to facilitate proactive public health measures. We advocate for paradigm shifts in environmental health research and governance from hazard identification to prevention-oriented governance, from isolated investigations to transdisciplinary convergence (e.g., exosomomics-AI integration), and from reactive regulation to anticipatory intelligence. Future efforts must prioritize high-risk ECs (e.g., per-and polyfluoroalkyl substances, microplastics, and endocrine disruptors), strengthen "big-data" national biomonitoring alongside "deep-mechanism" granular studies, and foster global data/knowledge sharing. This strategic roadmap aligns scientific rigor, digital innovation, and public health imperatives to catalyze sustainable EC mitigation, safeguard population health, and position China at the forefront of next-generation environmental governance and global stewardship. Embracing these changes will protect public health and promote a sustainable future. https://doi.org/10.1360/csb-2025-0307

Evaluation de l'exposition

Endocrine-disrupting chemicals in breast milk and early life exposure for infants in the United States,
Hazlehurst, M. F., Liu, C., Zheng, G., Koch, M., Schreder, E., Salamova, A. and Sathyanarayana, S., *Journal of Exposure Science & Environmental Epidemiology*, 2026/05// 2026, Vol. 36, no. 3, p. 550-558.

BACKGROUND: Breastfeeding can be a source of exposure to endocrine-disrupting chemicals (EDCs) for infants, but limited information exists on exposure to commonly used chemicals such as melamine and bisphenols in nursing infants in the US. OBJECTIVE: We aimed to measure a suite of EDCs in breast milk and evaluate exposure of nursing infants to these chemicals. METHODS: We analyzed EDCs in breast milk samples collected from 50 women in Seattle, Washington during 2019, including melamine, cyanuric acid, ammeline, ammelide, bisphenol A (BPA), 4-hydroxyphenyl sulfone (BPS), 4,4'-methylenediphenol, (4,4'-hexafluoroisopropylidene) diphenol, fluorene-9-bisphenol, and triclosan. We examined associations of infant age at sample collection and maternal characteristics with log10-transformed chemical concentrations using linear regression. Estimated daily intake (EDI) of each chemical through breast milk was calculated for infants 0-12 months old using our sample median chemical concentrations. RESULTS: We frequently detected (62-92%) melamine, cyanuric acid, BPA, BPS, and triclosan in breast milk. Median concentrations were 0.48 ng/mL melamine, 0.59 ng/mL cyanuric acid, 0.311 ng/mL BPA, 0.012 ng/mL BPS, and 0.072 ng/mL triclosan. Older infant age (>6 versus <6 months) was associated with lower melamine concentrations (-0.41, 95% CI: -0.80, -0.01). Maternal obesity was associated with higher BPA (0.68, 95% CI: 0.14, 1.23) and maternal overweight with higher triclosan (0.43, 95% CI: 0.06, 0.80). Other associations with participant characteristics were suggestive but not statistically significant. EDIs for infants in the average exposure scenario ranged by infant age from 40.3 to 72.8 ng/kg-bodyweight/day for melamine and 86.5-156 ng/kg-bodyweight/day for BPA. SIGNIFICANCE: We frequently detected melamine, cyanuric acid, BPA, BPS, and triclosan in breast milk. EDIs through breastfeeding were generally higher than for other exposure pathways (e.g., dermal uptake, dust ingestion or inhalation), and more work is needed to understand potential health effects of chronic infant exposures to even low levels of these ubiquitous chemicals through breast milk. IMPACT: This study adds to the limited research to date on endocrine-disrupting chemicals in breast milk, exposure among nursing infants in the US, and differences by infant and maternal characteristics, to further inform cumulative exposure assessment in infants and regulatory thresholds. Melamine, cyanuric acid, BPA, BPS, and triclosan were detected with high frequency in breast milk samples in our study, and our study suggests that breast milk is an important exposure pathway for these chemicals among nursing infants. Given the importance of breastfeeding for infant health, our study highlights the need to investigate potential health effects of these chronic exposures. https://doi.org/10.1038/s41370-026-00844-z

Targeting Plastic Exposure in Infertile Couples: A Pilot Intervention Study,
Hua, J. N., Rochester, J. R., Foley, J. M., Hahn, L. B., Min, M. Y., Kenfield, S. A., Smith, J. F. and Swan, S. H., *Toxics*, Mar 16 2026, Vol. 14, no. 3.

Endocrine-disrupting chemical (EDC) exposure from plastics and everyday products is widespread and linked to infertility. We conducted a 3-month uncontrolled feasibility pilot study among five idiopathically infertile couples to assess whether an intensive lifestyle intervention was associated with within-person changes in urinary EDC biomarkers and exploratory changes in reproductive parameters. The intervention was embedded in a film project ("The Plastic Detox") and integrated personalized education, product substitutions, at-home urine biomonitoring, sperm testing, and weekly coaching. Urine and semen samples were collected at baseline, 6 weeks, and 12 weeks. Linear mixed-effects models were used to estimate biomarker changes. BPA was designated a priori as the

primary biomarker endpoint. Directional reductions were observed in urinary bisphenol A (BPA), mono-n-butyl phthalate (MBP), and monobenzyl phthalate (MBzP) over the intervention period. Within-person reductions in products containing ingredients of concern were associated with lower BPA levels. Descriptive upward trends of semen parameters were observed, with the majority of the subfertile men testing >40 million motile sperm/ejaculate after the intervention. Participants had increased environmental health literacy, were more motivated to reduce exposures, and reported improved wellness endpoints. Four couples achieved pregnancy and live birth during follow-up; given the uncontrolled design and small sample size, these outcomes are presented descriptively. Overall, this pilot study demonstrates feasibility and measurable biomarker change, supporting evaluation in larger, controlled trials. https://doi.org/10.3390/toxics14030257

Mixture risk assessment of nine reproductive toxic chemicals affecting male sperm quality in a representative sample of children and adolescents living in Germany - results from the German Environmental Survey (GerES V),
Koelman, L., Lange, R., Kolossa-Gehring, M. and Murawski, A., *International Journal of Hygiene and Environmental Health*, May 2026, Vol. 274.

Reproductive health is declining globally, with growing evidence linking exposure to endocrine-disrupting chemicals during critical pregnancy stages to adverse male sexual development. This study assessed the cumulative risk of nine such chemicals-acrylamide, PCB 118, DEHP, DnBP, DiBP, BBzP, DiNP, DCHP, and DnPeP-and possible influencing factors such as age, socioeconomic status (SES), and region (former East vs. West Germany). We analyzed cross-sectional data from the German Environmental Survey for Children and Adolescents 2014-2017 (GerES V), including 1090 participants with complete urine and plasma samples. Using the Hazard Index (HI) method, which combines exposure levels with human biomonitoring guidance values, we found that 31% of participants had an HI above 1, indicating elevated risk from combined chemical exposure. Notably, 26% of these cases would have gone unnoticed in single-substance assessments. DnBP, DiBP, and acrylamide were the main contributors to overall risk. Stratified analyses revealed that younger children had higher HI levels than older ones. Children from lower SES backgrounds also showed higher risk compared to those from medium or high SES groups. Additionally, residing in former East Germany was associated with increased HI levels compared to former West Germany. These findings emphasize the importance of considering chemical mixtures in risk assessments and recognizing subgroup-specific vulnerabilities. Future assessments should expand the range of included chemicals and focus on high-risk groups-especially children, individuals with low SES, and residents of former East Germany-to better capture the scope of potential health impacts. https://doi.org/10.1016/j.ijheh.2026.114783

Identification and Characterization of Key Hazardous Substances in Precocious Puberty Children: An Internal Exposure Assessment in China's Typical Coastal Cities,
Li, X., Zhang, H., Zhao, X. Q., Ren, F., Jin, J., Peng, Y. H., Guo, C. C., Dai, Y. B., Cao, R., Geng, N. B., Chen, J. P. and Wu, L. D., *Environment & Health*, 2026.

Epidemiological studies indicate associations between exposures to endocrine-disrupting chemicals (EDCs) with reproductive disorders (e.g., early puberty). However, the scientific evidence remains limited, particularly in studies on clinically diagnosed precocious puberty (PP), and the specific pollutant drivers underlying this condition are poorly characterized. Identifying the key hazardous substances contributing to PP thus represents a critical research priority. This study conducted a population-based case-control study to profile the internal exposure to organic pollutants. Using a combination of liquid-liquid extraction (LLE) and solid-phase extraction, we performed suspect screening and nontargeted analysis with high-resolution mass spectrometry (HRMS) (liquid chromatography-/GC-Orbitrap HRMS). Nontargeted analysis revealed a broad spectrum of EDCs,

including polycyclic aromatic hydrocarbons, phthalate esters (PAEs), organophosphate esters (OPEs), phenols, amides, and acrylates. Differential analysis between cases and controls further highlighted several pollutant classes, such as organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), per- and polyfluoroalkyl substances (PFAS), phenols, and chlorinated paraffins. These pollutants were significantly elevated in the PP group. These findings provide new internal exposure data and methodological support for environmental health research. They also offer a scientific foundation for targeted source-control strategies to reduce children's exposure to harmful pollutants, supporting the broader public health objectives of "Healthy China 2030". https://doi.org/10.1021/envhealth.5c00693

Sociodemographic and Lifestyle Factors Associated with Historical Exposure to Persistent Flame Retardant Concentrations in a Spanish Cohort,
Linares-Ruiz, E., Pérez-Díaz, C., Pérez-Carrascosa, F. M., Gonzalez, S., Ramos, J. J., Salcedo-Bellido, I. and Arrebola, J. P., *Applied Sciences-Basel*, Feb 28 2026, Vol. 16, no. 5.

Featured Application The findings may contribute to the shaping of public health policies to identify population groups with elevated exposure to persistent flame retardants. Abstract The aim of this study was to estimate the historical exposure to a selection of polybrominated diphenyl ethers (PBDEs) and Dechlorane Plus (DP) concentrations and to identify the potential sociodemographic and lifestyle factors associated with this exposure. The study population (n = 134) was a subcohort of the GraMo Study, recruited in 2003-04 in Granada (Spain). Information on potential exposure-associated factors was collected through face-to-face interviews and a review of clinical records. Historical exposure was estimated by analyzing adipose tissue concentrations of 12 PBDEs and 2 DPs by means of gas chromatography coupled to a mass spectrometer. Data analyses included multivariable linear regression analyses. Median (interquartile range) pollutant concentrations ranged from 0.13 (0.09, 0.23) ng/g lipid for BDE-99 to 1.34 (0.92, 2.43) ng/g lipid for BDE-153. The body mass index was inversely associated with anti-DP, syn-DP, and BDE-153, -183, and -197 concentrations. Males exhibited higher levels of BDE-28, -47, -153, and -209 than females. Compared to non-manual workers, manual workers exhibited increased BDE-154, anti-DP, and syn-DP concentrations but lower BDE-28 levels. These findings highlight the elevated prevalence of PBDE/DP exposure and the heterogeneous exposure patterns observed across the study population. Further research is warranted to elucidate the long-term implications for human health. https://doi.org/10.3390/app16052346

Toxicité sur les animaux

Investigating ovarian effects of perfluorooctanoic acid in postpubertal pigs during thermal neutral and heat stress conditions,
Antwi-Boasiako, C., González-Alvarez, M. E., Buol, B. M., Adeyanju, O., Baumgard, L. H. and Keating, A. F., *Journal of Animal Science*, 2026 2026, Vol. 104.

Perfluorooctanoic acid (PFOA) is associated with disrupted female endocrine and reproductive function. In this study, the ovarian impact of PFOA exposure was investigated in postpubertal pigs housed in thermal neutral (TN) or heat stress (HS) environments. Gilts (n = 48) were housed in either TN conditions (21.0 +/- 0.10 degrees C) or cyclical HS (32.2 +/- 0.1 degrees C to 26.2 +/- 0.1 degrees C) for 19 days and assigned randomly to TN vehicle control (TC; n = 12), TN PFOA (TP; n = 12, 70 ng PFOA/kg), HS control (HC; n = 12), and HS PFOA (HP; n = 11; 70 ng PFOA/kg) treatments. Relative to TC, ovarian weight was decreased in TP (P = 0.03) and tended to be decreased in HP (P = 0.08). Follicular fluid estradiol tended (P = 0.08) to be decreased in HP relative to HC gilts. Dominant follicle size, vulva size, uterine weight, and follicular fluid progesterone level were not altered by treatment.

The number of ovarian primordial, primary, and secondary follicles was not affected by PFOA treatment, but tertiary follicles tended (P = 0.08) to be decreased by HS. In HP gilts, there were more primordial (P = 0.05), secondary (P = 0.002), and empty (P = 0.008) follicles and a tendency for increased primary (P = 0.06) and tertiary (P = 0.08) follicles compared to TC gilts. The abundance of ovarian microsomal epoxide hydrolase (EPHX1) was reduced in HP relative to TC (P = 0.005) and HC (P = 0.006) gilts. In TP gilts, 3 beta-hydroxysteroid dehydrogenase (3BHSD) was reduced (P = 0.02) and both cytochrome P450 family 19 subfamily A member 1 (CYP19A1) tended (P = 0.06) to be reduced, while 3BHSD tended to be reduced in HP compared to HC gilts (P = 0.09). Thus, there were ovarian impacts of PFOA exposure in TP gilts with some additive impacts in heat-stressed pigs. Perfluorooctanoic acid (PFOA), a persistent environmental pollutant that bioaccumulates in vivo primarily through contaminated food and water, is associated with disruptions to female endocrine and reproductive function, but whether this also occurs in a porcine model is not known. In addition, heat stress (HS) impairs female reproduction and it has the potential to be additive to PFOA exposure. In this study, the hypothesis explored was that PFOA would impact ovarian phenotypic variables and steroidogenic metrics and that these effects would be augmented by HS. Some ovarian endpoints altered by PFOA were independent from HS but others, including abundance of ovarian proteins, were influenced by ambient temperature. Heat stress and perfluorooctanoic acid exposure negatively affect ovarian function with some additive effects noted. There is a need to identify mechanisms through which environmental stressors compromise female reproduction. https://doi.org/10.1093/jas/skag062

Sex-specific disruption of estrogen receptor alpha (ERα) density in the social brain neural network by Firemaster 550,
Cao, J., Gillera, S. E. A., Marinello, W. P. and Patisaul, H. B., *Journal of the Endocrine Society*, 2026/04// 2026, Vol. 10, no. 4, p. bvag050.

We investigated how developmental exposure to the commercial flame retardant (FR) mixture Firemaster 550 (FM 550) affects estrogen receptor alpha (ERα) expression in key brain regions related to sociosexual behavior. We used prairie voles, a socially monogamous, biparental rodent species of high translational human relevance. This study used adult siblings from a prior behavioral study showing developmental FM 550 exposure impaired a range of socioemotional behaviors in adults including loss of partner preference in males. Dams were exposed to FM 550 (500, 1000, or 2000 µg/day) via subcutaneous injections throughout gestation, and pups were directly exposed from birth to weaning. ERα immunoreactive (ERα-ir) neuron numbers and mRNA expression levels were quantified in subregions of the social brain neural network (SBNN). As anticipated, FM 550 impacts were sex-, dose-, and region-specific, with FM 550 tending to increase ERα-ir cell numbers in the anterior hypothalamus regardless of sex, but decrease them in the female mediobasal hypothalamus, amygdala, and extended amygdala. These studies demonstrate that developmental FR exposure impacts adult SBNN ERα availability and provide support that disrupted ERα action in the SBNN may be a mechanism underlying disruption of socioemotional behavior, energy balance, and related neuroendocrine physiology. Impacted ERα neuronal populations are also influenced by other receptors, neuropeptides, neurosteroids, and signaling molecules to govern prosocial behaviors, which is the ongoing direction of this work. Collectively, these data add to growing evidence that FM 550 FRs are neuroendocrine disruptors that can induce persistent impacts across developing socioemotional pathways and systems. https://doi.org/10.1210/jendso/bvag050

The effects of desflurane on male rat reproductive hormones, testicular tissue, and sperm morphology: an experimental study,
Dogru, S., Dogru, H. Y., Tapar, H., Arici, A. and Suren, M., *Bmc Anesthesiology*, Feb 6 2026, Vol. 26, no. 1.

Background Desflurane is a widely used inhalational anesthetic known for its advantageous properties in clinical settings. This study aimed to investigate the effects of desflurane inhalation on male reproductive hormones, testicular tissue integrity, and sperm morphology in a rat model. Methods Thirty male rats were allocated into six experimental groups: Control group (C): Administered 2 L/min of O-2 for 18 minutes daily over seven days. Group D1: Exposed to 1 minimum alveolar concentration (MAC) of desflurane and 2 L/min of O-2 for 18 minutes daily over seven days. Group D2: Received the same treatment as Group 1 for seven days, followed by a seven-day recovery period without intervention. Group D3: Administered 1 MAC desflurane and 2 L/min of O-2 for 18 minutes daily over 14 days. Group D4: Received the same treatment as Group 3 for 14 days, followed by a seven-day recovery period without intervention. Group D5: Administered the same treatment as Group 3 for 14 days, followed by a 14-day recovery period without intervention.Biochemical analyses were conducted to measure serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and inhibin B. Histopathological evaluations were performed to assess testicular tissue integrity, and sperm morphology was examined to identify abnormalities. Results Significant histopathological damage was observed in all experimental groups compared to the control group ($p < 0.05$). The proportion of morphologically abnormal spermatozoa was significantly higher in Groups D2, D3, D4, and D5 compared to the control group ($p = 0.030$, $p = 0.002$, $p < 0.001$, and $p = 0.016$, respectively). Compared to the control group, serum FSH levels showed a slight decrease across desflurane-exposed groups (ranging from -1.4% to +4.02%). The LH levels demonstrated a gradual reduction of approximately 0.32%-7.38%, while serum testosterone concentrations increased markedly, reaching up to 178% of the control level in the D4 group. Inhibin-B levels exhibited a progressive elevation of nearly 23-95% compared to control group. Conclusion Chronic inhalation of desflurane, a modern inhalational anesthetic, was found to adversely affect testicular histology, sperm morphology, and the regulation of male reproductive hormones in rats. These findings highlight potential reproductive toxicity associated with prolonged desflurane exposure. https://doi.org/10.1186/s12871-026-03668-4

Endocrine and metabolism modulating effects of paracetamol: From in vitro signaling to in vivo metabolic reprogramming in male mice,
Entezari, B., Bozdag, D., Buhur, A., Sabuncuoglu, S., Yavasoglu, A. and Gurer-Orhan, H., *Toxicology*, Aug 2026, Vol. 524.

Obesity is a major global health challenge associated with a cluster of comorbidities, including metabolic syndrome and type 2 diabetes, necessitating a deeper understanding of the environmental factors contributing to this epidemic. This study investigated the in vitro adipogenic/lipogenic potential of paracetamol and its in vivo endocrine and metabolic modulating effects following prenatal exposure. Using the 3T3-L1 preadipocyte model, cells were exposed to paracetamol at physiologically relevant concentrations. Results demonstrated that paracetamol promoted lipid accumulation and upregulated G3PDH activity. Furthermore, low concentrations significantly increased the protein expression of key adipogenic regulators (PPAR gamma, C/EBP alpha, LPL, and SREBP1), suggesting interference with transcriptional cascades governing adipogenesis and lipogenesis. To assess in vivo effects, pregnant CD1 mice were exposed to paracetamol at three human relevant doses (Cmax/10, Cmax, and Cmax ×10). In male F1 offspring, prenatal exposure resulted in increased anogenital distance and a higher incidence of sperm morphological abnormalities, indicating reproductive developmental alterations despite unchanged circulating hormone levels. Metabolically, offspring exhibited dyslipidemia characterized by elevated serum triglycerides and total cholesterol. Although body weight and glucose tolerance remained unaffected, lipidomic profiling of epididymal adipose tissue revealed pronounced remodeling, including the accumulation of neutral lipids and altered membrane phospholipid composition. This was

accompanied by the upregulation of the adipogenic genes Ppar gamma, Lpl, and Fasn in adipose tissue. Collectively, these findings suggest that paracetamol may act as an endocrine modulator and metabolic disruptor when exposed prenatally, inducing latent metabolic dysregulation that may predispose offspring to metabolic syndrome later in life, even in the absence of overt obesity. https://doi.org/10.1016/j.tox.2026.154468

Effects of Maternal Tetramethyl Bisphenol F Exposure on Neurodevelopment and Behavior in Mouse Offspring,
Hwang, I., Kim, S. and Jeung, E. B., *International Journal of Molecular Sciences*, Apr 5 2026, Vol. 27, no. 7.

Bisphenol A (BPA) has long been used in plastics, resins, and food packaging materials; however, extensive research has demonstrated its reproductive, developmental, and endocrine-disrupting effects. Consequently, BPA has been increasingly restricted and replaced with structural analogues. Among these, tetramethyl bisphenol F (TMBPF) has emerged as one of the most widely used substitutes, particularly in epoxy resins and food-can coatings. Although initially regarded as a safer alternative, accumulating evidence suggests that TMBPF may exert multiple toxicological effects, raising concerns about its potential developmental neurotoxicity. The present study aimed to investigate the neurodevelopmental effects of TMBPF using both in vitro and in vivo approaches. First, a developmental neurotoxicity assay employing Sox1-GFP mouse embryonic stem cells was used to evaluate cytotoxicity using the cell counting kit-8 assay and neural differentiation based on green fluorescent protein (GFP) fluorescence intensity. The results indicated developmental neurotoxic potential according to the established discrimination index. Subsequently, pregnant and lactating mice were exposed to TMBPF daily from gestational day 10.5 to postnatal day 20, and their offspring were assessed for behavioral performance as well as changes in the expression of neurodevelopment-related genes in the brain. Behavioral analyses encompassed multiple domains, including memory and learning, social behavior, anxiety-related responses, and spontaneous locomotor activity, suggesting alterations in these functional outcomes. Molecular analyses further demonstrated changes associated with dopaminergic and cholinergic signaling, synaptic plasticity, neuronal activity markers, neuropeptides, and inflammatory pathways. Collectively, these findings provide the first evidence in a mammalian model that maternal exposure to TMBPF may influence offspring neurodevelopment. These findings suggest potential implications for human exposure to TMBPF, particularly through food-contact materials, and warrant further mechanistic and dose-response studies. https://doi.org/10.3390/ijms27073299

Diethyl phthalate-induced oxidative stress, genotoxicity, and thyroid hormone disruption in female Wistar rats,
Kömürcü, A. and Yavas, M. C., *Food and Chemical Toxicology*, Jun 2026, Vol. 212.

Background: Diethyl phthalate (DEP), a common plasticizer in cosmetics and personal care products, is known to induce oxidative stress and endocrine disruption. Its widespread use raises concerns about thyroid toxicity. Objective: This study aimed to evaluate the genotoxic and endocrine effects of subacute DEP exposure on thyroid tissue in female Wistar albino rats using thyroid hormones, oxidative stress markers, DNA damage, and histopathology. Methods: Twenty-eight female Wistar albino rats were divided into four groups (n = 7): control, 100 mg/kg, 300 mg/kg, and 600 mg/kg DEP. DEP was administered orally for 21 days. DNA damage was assessed by Comet Assay, oxidative stress markers (TAS, TOS, OSI) were measured, and serum TSH, T3, and T4 levels were determined by ELISA. Body weights were monitored, and thyroid tissues were examined histologically. Results: Compared to the control group, T3 and T4 levels decreased ($P < 0.05$), TSH levels increased ($p < 0.05$), TAS levels decreased ($p < 0.05$), and TOS and OSI levels increased ($p < 0.05$). Comet Assay showed dose-

dependent DNA damage (tail DNA%, p < 0.05). With higher DEP doses, thyroid tissue histopathology changed significantly. Conclusion: Subacute DEP exposure causes dose-dependent genotoxicity, oxidative stress, and endocrine disruption in thyroid tissue. These findings emphasize the need to limit environmental and human DEP exposure. https://doi.org/10.1016/j.fct.2026.116031

Maternal Bisphenol S Exposure Impairs Testicular Development and Sperm Function in Male Offspring by Disrupting the Immune-Endocrine Network,
Li, B., Tian, Y., Wu, X., Gong, Z., Liang, X., Zhang, J., Hu, Y., Ji, X. and Yue, H., *Small*, Vol. n/a, no. n/a, p. e13075.

Bisphenol S (BPS), a widely used substitute for bisphenol A, is an environmental contaminant with endocrine-disrupting properties. However, the transgenerational impact of maternal BPS exposure during gestation on male offspring reproductive health and the underlying molecular mechanisms remains unknown. This study shows that gestational exposure of mice to environmentally relevant concentrations of BPS (3, 30, and 300 μg/kg) dose- and time-dependently impairs testicular development and sperm function in male offspring. Integrated transcriptomic, physiological, and molecular analyses revealed that maternal BPS exposure remodeled the testicular transcriptome and disrupted the immune-endocrine crosstalk within the testis. This disruption was characterized by the aberrant activation of immune and inflammatory pathways, including antigen presentation, concomitant suppression of steroidogenic and metabolic processes, and induction of the renin-angiotensin system. Deconvolution analysis identified loss of Leydig cells and increased Tcell infiltration, and quantitative realtime PCR validated the dysregulation of key hub genes such as Ren1, H2-D1, Naip6, Tlr1, H2-M3, Pycard, B2m, H2-Aa, Naip1, and Cd74. Notably, western blotting revealed that HLA-DPB1, a key component of the antigen presentation pathway, was significantly downregulated at the protein level in testicular tissues. Immunofluorescence co-localization with cell-specific markers defined the precise cellular localization in the testis. Collectively, these multilevel disruptions resulted in impaired seminiferous epithelial cyclicity, enhanced interstitial collagen deposition in the testes, and severe deficits in sperm motility. Our findings reveal a novel transgenerational mechanism underlying BPS-induced testicular injury and provide robust experimental evidence of the reproductive toxicity of environmentally relevant BPS in male offspring. https://doi.org/10.1002/smll.202513075

Maternal exposure to phthalates and nanoplastics, isolated or combined: Impacts on placental structure, development, and antioxidant defense as a trigger for maternal-fetal adversities,
Magosso, N., Souza, P. V., Moreira, M. F., Rocha, V. A., Fioretto, M. N., Pinha, V. C., Maia, G. A., Maria, V., Barata, L. A., Frigoli, G. F., Fernandes, G. S. A., Arena, A. C. and Scarano, W. R., *Reproductive Toxicology*, Aug 1 2025, Vol. 135.

The placenta is an essential maternal-fetal organ for the healthy development of the fetus, linking maternal and fetal circulations. Endocrine disrupting chemicals (EDCs), such as phthalates derived from plastic residues, may impair offspring development and increase the risk of metabolic disorders. Plastics also degrade into microplastics (MPs) and nanoplastics (NPs), which can cross the placenta, carrying EDCs and impacting fetal development. The objective of this study was to investigate whether gestational exposure to a phthalate mixture (PM) and NPs interferes with the maternal-fetal interface, altering female reproductive efficiency and placental morphophysiology. Pregnant SD rats were divided into 6 groups: CTR(control; vehicle), T1(20 mu g/kg/day-PM), T2(200 mg/kg/day-PM), T3(1 mg/kg/day NPs-100nm), T4(20 mu g/kg/dayPM+1 mg/kg/day-NPs-100nm), and T5(200 mg/kg/day-PM+1 mg/kg/day-NPs-100 nm). Treatment was administered orally from gestational day 5 (GD5) to GD20. At GD20, 5-8 rats from each group were anesthetized and underwent laparotomy, and blood, ovaries, uterus, and placentas were analyzed. There was an increase in pre-implantation

loss in T3, T4 and T5 groups, a reduction in placental weight, and an increase in placental efficiency in male offspring in T3 group. An increase in the number of fetuses small for gestational age was observed in T3 and T5 vs. C. Furthermore, the treatment caused an increase in the expression of targets related to trophoblast cell differentiation in T5, and growth factors related to angiogenesis in the placenta in T3 and T4 groups. There was a decrease in TBARS, SOD, and GSTpi levels in T2, while CAT increased in T3, suggesting that these pollutants modulate placental gene expression and energy metabolism. https://doi.org/10.1016/j.reprotox.2025.108930

Toxicological impact of tetrabromobisphenol-A on pregnant rats: Morphological, biochemical, and histopathological investigations,
Özkan, M., Inkaya, E. N., Koçkaya, E. A. and Barlas, N., *Toxicology and Industrial Health*, May 2026, Vol. 42, no. 5, p. 178-197.

Tetrabromobisphenol-A (TBBPA) is found in high concentrations in textiles, plastic polymers, flame retardants, and various industrial products. In this maternofetal study, we aimed to evaluate the potential effects of TBBPA on the mother, fetus, and placenta in pregnant rats. In the experimental design, three different gestational days (GD10, GD15, and GD20) were selected for evaluation in pregnant rats. For each gestational period, one control group (corn oil) and three TBBPA dose groups (20, 200, and 400 mg/kg) were established, resulting in a total of 12 experimental groups. Each group included six pregnant rats. We hypothesized that TBBPA exposure would lead to alterations in maternal and fetal hormonal and placental parameters when evaluated across different doses and gestational days. Placenta, kidney, liver, and ovary tissues were examined histopathologically. Levels of follicle-stimulating hormone (FSH), progesterone, luteinizing hormone (LH), and estrogen were analyzed. Estrogen from ovarian homogenates and testosterone from testicular homogenates of GD20 fetuses were also measured. We detected statistically significant differences in placental and fetal data. However, no severe effects were observed. Serum FSH levels were elevated in the GD20 group receiving 400 mg/kg, whereas LH levels increased in the GD15 group at both 200 and 400 mg/kg compared to controls. In GD20 female fetuses, estrogen levels decreased at 20 mg/kg but increased at 200 mg/kg relative to the control group. Histopathological examination of placental tissue revealed congestion, degeneration in the labyrinth region, cytoplasmic dissolution and pyknosis in giant cells, and degeneration in spongiotrophoblasts. No severe systemic toxicity was observed in our study. However, the mild to moderate level changes detected highlight the need for further investigation of TBBPA, especially considering the uncertainties regarding its effects during pregnancy. https://doi.org/10.1177/07482337261438207

Combined Exposure to Endocrine Disruptors, BPA and BP-3, during Pregnancy and Lactation Alters Postnatal Body Mass, Growth, White Adipose Tissue Morphology, and Adipogenic Gene Expression in a Sex-Specific Manner,
Raticova, K., Howanski, J., Fink, B., Roder, S., Bauer, M., Schumacher, A., Zenclussen, A. C. and Kretschmer, T., *Environment & Health*, 2026.

Endocrine-disrupting chemicals (EDCs) like bisphenol A (BPA) and benzophenone-3 (BP-3) are omnipresent and previously linked to various metabolic disorders. As EDC exposure already begins during prenatal development, we investigated the effects of BPA and BP-3 exposure during gestation and lactation using a murine model on adipogenesis and metabolic pathways in white adipose tissue (WAT) in the offspring. We monitored postnatal body mass and analyzed the morphology and gene expression of WAT in adult male and female offspring. BPA- and BPA+BP-3-exposed males showed an increase in body mass in early adulthood, whereas BP-3-exposed females presented a decreased growth rate later in life. We identified altered adipocyte area and distribution, suggesting hyperplasia in the WAT of BPA and BPA+BP-3-exposed males. Gene expression analysis showed Pparg

upregulation in BPA+BP-3-exposed males and Fabp4 and Adipoq downregulation in BP-3-exposed females. Sex-specific associations between gene expression, adipocyte area, and body mass in controls were disrupted by EDC exposure. Our findings suggest increased postnatal body mass and Pparg-mediated WAT hyperplasia in BPA+BP-3-exposed male mice. Fabp4 and Adipoq downregulation may be responsible for counteracting the BP-3-induced metabolic dysregulation in females. This calls for consideration of sex-specific differences of endocrine disruption in the future development of preventive and therapeutic targets for metabolic disorders. https://doi.org/10.1021/envhealth.5c00679

Exposure to Bisphenol A and Z causes DNA damage and testicular histopathology impairing male fertility,
Rehman, H. U., Nadeem, A., Mukhtar, N., Ali, M. M., Mujahid, H., Shabbir, M. Z. and Javed, M., *Toxicology and Industrial Health*, May 2026, Vol. 42, no. 5, p. 198-206.

Bisphenol analogues are commonly found in various consumer products such as food and beverage containers, electronic devices, toys, paper products, water pipes, and medical equipment. These compounds have been shown to disrupt endocrine function and exert harmful effects on multiple body organs. To investigate the tissue- and DNA-damaging effects of varying oral doses of Bisphenol Z (BPZ), a study was conducted on Wistar rats over a 4-week period. After 28 days, the rats were dissected, and tissue samples were collected. Tissue histology, Comet assay, and real-time PCR were performed to assess the effects of BPZ at the tissue and genomic levels. Sperm count and motility were significantly reduced in groups exposed to higher doses of BPZ (mean +/- SD: 27.00 +/- 7.94 and 4.33 +/- 0.43, respectively). Morphologically abnormal sperm, including deformed heads and curly tails, were observed. The Comet assay on testicular tissues from rats treated with higher BPZ doses showed clear signs of DNA fragmentation. Histopathological analysis revealed narrowing of the interstitial spaces and constriction of the epididymal lumen. Additionally, down regulation of the Protamine1 gene was observed in rats receiving higher doses of BPZ, significantly associated with spermatogenesis. Our findings not only highlight the severity of BPZ's toxic effects but also emphasize that these chemicals are unsafe in any analogue form. https://doi.org/10.1177/07482337261438341

Female reproductive toxicity of chronic exposure to perfluorohexane sulfonate (PFHxS) under the confounding factor of dietary protein deficiency,
Suramya, S., Javed, M., Ahmad, B. and Raisuddin, S., *Reproductive Toxicology*, May 2026, Vol. 142.

Per-and polyfluoroalkyl substances (PFHxS) is a perfluoroalkyl substance (PFAS). PFASs are ubiquitous and persistent, due to their bioaccumulative tendency, posing long-term health-related concerns. Human exposure to PFHxS is mainly via contact and ingestion. Diet and environmental exposure to toxicants significantly affect fertility outcomes. Nutrition is also a confounding factor in the toxicity of drugs and chemicals. In this study, we investigated the effect of chronic exposure to PFHxS under low protein diet. A low-protein diet combined with exposure to PFHxS for 90 days via drinking water in female rats caused significant hormone changes, inflammation, and fibrosis in ovarian tissue. Elevated anti-Mullerian hormone levels, downregulated expression of CYP19A1 and follicle stimulating hormone receptor, and upregulated CYP17A1, indicated impaired folliculogenesis and steroidogenesis. Forkhead box protein O1 (FOXO1) immunostaining and gene expression highlighted metabolic and oxidative stress due to PFHxS exposure. The histological analysis revealed collagen deposition surrounding growing follicles, along with enhanced transforming growth factor beta 1 (TGF-beta 1) expression, suggesting a progression of fibrosis. TUNEL assay and Bax immunostaining revealed enhanced granulosa cell apoptosis. Ultrastructural analysis showed changes in the endoplasmic reticulum and mitochondria. These results demonstrate the effect of dietary protein

deficiency on PFHxS toxicity, contributing to ovarian injury and associated disorders. https://doi.org/10.1016/j.reprotox.2026.109213