Bulletin de veille Perturbateurs Endocriniens N°31 – Août 25

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

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

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Exposition professionnelle

Phthalate Metabolites and Their Relationship with Abdominal and General Obesity: Evidence from the Aragon Workers' Health Study (AWHS),
Akritidis, J., Mérida, D. M., Torrijo-Belanche, C., Moreno-Franco, B., Gimeno-Ruiz, S., Rey-García, J., Morales-Suarez-Varela, M. and Guallar-Castillón, P., *Nutrients*, May 30 2025, Vol. 17, no. 11.

BACKGROUND/OBJECTIVES: Phthalates are endocrine-disrupting chemicals that are commonly used in plastic consumer products and food packaging, with growing evidence suggesting that they have a potential role in obesity. This study aimed to investigate the association between urinary concentrations of phthalate metabolites and both general and abdominal obesity among adult

males in Spain. METHODS: We analysed data from 1124 male participants of the Aragon Workers' Health Study (AWHS) collected between 2011 and 2014 in Zaragoza, Spain. Eleven urinary phthalate metabolites were measured and adjusted for creatinine levels. Multivariate logistic regression models were used to evaluate associations between phthalate exposure and general and abdominal obesity, controlling for dietary and lifestyle factors. Dose-response relationships were explored using restricted cubic spline models. RESULTS: Higher urinary concentrations of di(2-ethylhexyl) phthalate (∑DEHP) and two of its metabolites-mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)-were significantly associated with general obesity. The adjusted odds ratios were: ∑DEHP [OR = 1.26; 95% CI: 1.01, 1.58], MEOHP [OR = 1.24; 95% CI: 1.00, 1.53], and MEHHP [OR = 1.26; 95% CI: 1.03, 1.55]. In contrast, mono-isobutyl phthalate (MiBP) was inversely associated with abdominal obesity [OR = 0.73; 95% CI: 0.57, 0.93]. CONCLUSIONS: These findings suggest a positive association between exposure to DEHP and its metabolites and general obesity. This highlights the potential importance of environmental exposures as modifiable factors in obesity prevention and supports the need for further investigation in nutritional and public health contexts. https://doi.org/10.3390/nu17111869

Phthalate Metabolites and Their Relationship with Abdominal and General Obesity: Evidence from the Aragon Workers' Health Study (AWHS).
Akritidis, J. a.-O. X., Mérida, D. a.-O., Torrijo-Belanche, C. a.-O., Moreno-Franco, B., Gimeno-Ruiz, S. a.-O., Rey-García, J. a.-O., Morales-Suarez-Varela, M. a.-O. and Guallar-Castillón, P. a.-O., no. 2072-6643 (Electronic).

BACKGROUND/OBJECTIVES: Phthalates are endocrine-disrupting chemicals that are commonly used in plastic consumer products and food packaging, with growing evidence suggesting that they have a potential role in obesity. This study aimed to investigate the association between urinary concentrations of phthalate metabolites and both general and abdominal obesity among adult males in Spain. METHODS: We analysed data from 1124 male participants of the Aragon Workers' Health Study (AWHS) collected between 2011 and 2014 in Zaragoza, Spain. Eleven urinary phthalate metabolites were measured and adjusted for creatinine levels. Multivariate logistic regression models were used to evaluate associations between phthalate exposure and general and abdominal obesity, controlling for dietary and lifestyle factors. Dose-response relationships were explored using restricted cubic spline models. RESULTS: Higher urinary concentrations of di(2-ethylhexyl) phthalate (∑DEHP) and two of its metabolites-mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP)-were significantly associated with general obesity. The adjusted odds ratios were: ∑DEHP [OR = 1.26; 95% CI: 1.01, 1.58], MEOHP [OR = 1.24; 95% CI: 1.00, 1.53], and MEHHP [OR = 1.26; 95% CI: 1.03, 1.55]. In contrast, mono-isobutyl phthalate (MiBP) was inversely associated with abdominal obesity [OR = 0.73; 95% CI: 0.57, 0.93]. CONCLUSIONS: These findings suggest a positive association between exposure to DEHP and its metabolites and general obesity. This highlights the potential importance of environmental exposures as modifiable factors in obesity prevention and supports the need for further investigation in nutritional and public health contexts. FAU - Akritidis, Jordan https://doi.org/10.3390/nu17111869

Case Report: Toxic tubulointerstitial nephropathy with lipofuscin deposition - the potential cause of occupational Bisphenol-A exposition,
Bidiga, L., Csonka, T., Méhes, G., Markóth, C., Hutkai, D. and Mátyus, J., *Pathol Oncol Res*, 2025, Vol. 31, p. 1612046.

This case study delves into the link, between exposure to Bisphenol A (BPA) and kidney issues filling a gap in human focused research found in studies. The individual, a 72-year man with a history of BPA exposure in a plastics manufacturing facility experienced a gradual decline in kidney function

over 18 months. Medical tests showed kidney disease with a buildup of lipofuscin in renal tubular cells upon examination. This discovery suggests a connection between BPA exposure and kidney damage underscoring the need for investigation. The lack of human based evidence highlights the importance of research to understand the toxic effects of BPA on the kidneys. In addition, to its implications this case emphasizes the importance of improving safety protocols and raising awareness among healthcare professionals in relevant work environments to reduce potential health risks associated with BPA exposure. https://doi.org/10.3389/pore.2025.1612046

Children's environmental and occupational exposures to pesticides in low- and middle-income countries rural areas - an elephant in the room,
Buralli, R., Nazli, S. N., Cordoba, L., Quiros-Alcala, L., Hyland, C., Muñoz-Quezada, M. T., Farías, P. and Handal, A. J., no. 1879-1026 (Electronic).

In rural areas of Low- and Middle-Income Countries, children are regularly exposed to pesticides through various environmental, para-occupational, and occupational pathways, often connected to family-based agricultural activities. Work and living spaces are commonly intertwined, increasing the likelihood of unintentional pesticide exposure among children, including before birth. This commentary explores how such wide-spread exposures to these pervasive chemicals occur - even before birth, and affect critical aspects of child health and development through life. Using the history of Zeca, a child living in rural Brazil whose asthma worsens due to pesticide applications near his home, this discussion paper illustrates how this critical issue is deeply embedded in daily life in many agricultural communities. However, these risks are frequently overlooked in clinical assessments, health surveillance, and policy responses. We discuss how broader structural conditions contribute to children's exposure to pesticides, including poverty, lack of healthcare access, weak surveillance or enforcement of occupational and environmental protections, and the chemical colonialism. These patterns reflect entrenched social and environmental injustices that disproportionately affect rural children. Thus, we call for a coordinated and systemic response involving stronger regulation, enhanced health surveillance and management, support for safer and more sustainable agricultural practices, and the inclusion of rural communities in decision-making processes. The protection of children from harmful pesticide exposure must be recognized as a public health priority and a matter of social and environmental justice.
https://doi.org/10.1016/j.scitotenv.2025.179887

Occupational Exposure to Pesticides Among Farmworkers in Morocco: A Study Framework for Endocrine and Epigenetic Effect Assessment,
Chbihi, K., Menouni, A., Berni, I., Chetouani, H., Abou-Said, S., Amellah, A., Lebegge, R., Verscheure, E., Vanoirbeek, J., Duca, R. C., Godderis, L. and El Jaafari, S., *Toxics*, Apr 25 2025, Vol. 13, no. 5.

Pesticides are compounds of major use in agriculture worldwide. Nevertheless, many pesticide chemicals are classified as endocrine disruptors and potentially carcinogens. Farmers and farmworkers are particularly exposed and are at high risk of developing health-related impairments. In Morocco, the lack of awareness towards pesticide hazards and the inappropriate application of safety measures might increase the exposure as well as the risks of health concerns. In this paper, we present the framework of a study designed to assess pesticide exposure among Moroccan farmers and farmworkers and to evaluate potential health effects, namely endocrine and epigenetic impacts. Human biological monitoring will be conducted to determine pesticide levels in urine following the development and validation of sensitive chromatography methods (SPE, UPLC-MS/MS). Biomarkers of exposure include a set of parent and metabolite pesticide compounds (organophosphates, pyrethroids, triazines and urea-based pesticides). Thyroid and reproductive hormones (TSH, T-3, T-4, FSH and LH) as well as global and specific DNA methylation markers (5-mC,

5-hmC, N-6-mA, THRB and LHR) are selected as biomarkers of effects. This provides guiding steps and methods to perform reliable exposure evaluation and health impact assessment. This study aims to expand the current knowledge on the endocrine and epigenetic risks related to pesticides, especially in low- and middle-income countries. https://doi.org/10.3390/toxics13050340

Changes in serum perfluorooctane sulfonic acid and perfluorohexane sulfonic acid concentrations in firefighters accessing a voluntary perfluoroalkyl and polyfluoroalkyl substances reduction treatment program,
Delaere, I., Harris, K., Gaskin, S., Tefera, Y., Mitchell, K., Springer, D. and Mills, S., no. 1873-6750 (Electronic).

BACKGROUND: In 2018/2019 a voluntary baseline biomonitoring survey (n = 916) identified firefighters at a fire station with substantially elevated serum perfluorooctane sulfonic acid (PFOS) and perfluorohexane sulfonic acid (PFHxS) concentrations. The South Australian Metropolitan Fire Service (SAMFS) initiated a voluntary treatment program (VTP) to address the impact of these exposures (participants n = 19). At the conclusion of the VTP, a retrospective analysis of a de-identified and coded serum PFOS and PFHxS concentration spreadsheet was conducted independently of the VTP. OBJECTIVE: This study reports longitudinal changes in serum PFOS and PFHxS concentrations and compares participants accessing the VTP with an observational group that did not seek treatment. METHODS: The dataset included a treatment group (n = 19) and an observation group (n = 9). The treatment group was further subdivided into three subgroups: (1) plasma donation (n = 2), (2) cholestyramine administration (n = 12), and (3) a combination of plasma donation and cholestyramine administration (n = 5). Repeat samples identified participants' maximum and minimum serum PFOS and PFHxS concentrations. The calculations only included data from participants whose serum PFOS and PFHxS concentrations decreased. Apparent half-lives were estimated using one-compartment first-order elimination kinetics. The study did not conduct statistical comparisons; conclusions were drawn based on visual observations. RESULTS: The average change in serum concentration for the treatment group (PFOS: maximum decrease of 162 ng/mL, annual decrease of 41 %, with a half-life of 1.2 years; PFHxS: maximum decrease of 37 ng/mL, annual decrease of 32 %, with a half-life of 2.5 years) was compared with the observation group (PFOS: maximum decrease of 41 ng/mL, annual decrease of 12 %, with a half-life of 7.3 years; PFHxS: maximum decrease of 6 ng/mL, annual decrease of 10 %, with a half-life of 9.4 years). CONCLUSION: This study shows that participants who received treatment eliminated PFOS and PFHxS from their serum at a greater rate than the observation group.
https://doi.org/10.1016/j.envint.2025.109609

Per- and polyfluoroalkyl substances (PFAS) and microRNA: An epigenome-wide association study in firefighters,
Furlong, M. A., Liu, T., Jung, A., Beitel, S., Hughes, J., Krause, R., Graber, J. M., Calkins, M. M., Calafat, A. M., Botelho, J. C., Huentelman, M., Gulotta, J., Goodrich, J. M. and Burgess, J. L., *Environmental Research*, Aug 15 2025, Vol. 279.

The occupation of firefighting is classified as a Group 1 carcinogen. Increased cancer risk among firefighters may be partly attributable to increased occupational exposure to a range of chemicals, including per- and polyfluoroalkyl substances (PFAS). Some PFAS are known and suspect human carcinogens. Investigating epigenetic response to these PFAS exposures in firefighters may help to identify biological pathways of specific cancers, and previously unidentified health outcomes that are associated with PFAS. We therefore investigated the associations of serum PFAS concentrations with miRNA expression in firefighters. Serum samples collected from 303 firefighters from 6 sites across the USA were analyzed for 9 PFAS along with miRNA expression. Covariate-adjusted linear

regression was used to estimate associations between log PFAS and miRNA expression, with false discovery rate (FDR) set to 0.05 for significance, and an exploratory cutoff of FDR q < 0.20. Gene set enrichment analysis (GSEA) was performed using miRTarBase's miRWalk pathways. Age, race-ethnicity, BMI, fire department, and sex were controlled for in all models. At FDR<0.05, the linear isomer of perfluorooctane sulfonic acid (PFOS) was inversely associated with miR-128-1-5p expression (Beta = -0.146, 95 % CI -0.216, -0.076). At a relaxed FDR of 0.20, we observed inverse associations for the sum of branched isomers of PFOS (Sm-PFOS) with 5 miRNAs (let-7d-5p, let-7a-5p, miR-423-5p, let-7b-5p, miR-629-5p). Several pathways were enriched for multiple PFAS, including those correlated with certain cancers, blood diseases, thyroid disorders, autoimmune disorders, and neurological outcomes. Some PFAS in firefighters were found to be associated with alteration of miRNA consistent with increased risk for a range of chronic diseases.
https://doi.org/10.1016/j.envres.2025.121766

Occupational Benzene Exposure and Risk of Male Genital Cancers: A Systematic Review and Meta-Analysis,
Godono, A., Quattrocolo, A., Caradonna, R., Picciaiola, M. V., Boffetta, P. and Seyyedsalehi, M. S., *American Journal of Industrial Medicine*, Aug 2025, Vol. 68, no. 8, p. 666-678.

BackgroundBenzene is an established Group 1 carcinogen due to its leukemogenic properties. Recent studies suggest that occupational benzene exposure may be associated with solid cancers. However, little is known about its association with male genital cancers. We aimed to summarize the scientific evidence on occupational benzene exposure and the risk of male genital cancers.MethodsWe searched for relevant articles in three electronic databases. Methodological quality and the certainty of evidence were evaluated using a modified version of the Newcastle-Ottawa Scale (NOS) and Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment tool. We performed pooled and stratified meta-analyses, as well as meta-regressions to explore potential sources of heterogeneity.ResultsThirty-one publications were included. Pooled results of incidence and mortality for prostate and testis cancer did not indicate a significant association with occupational benzene exposure. A borderline association was found for the incidence of prostate cancer (standardized incidence ratio (SIR): 1.07, 95% CI 0.97-1.19). Subgroup analyses stratified by study design and study quality revealed significant heterogeneity, with case-control (relative risk (RR): 1.19, 95% CI 1.04-1.36) and high-quality studies (RR: 1.22, 95% CI 1.14-1.31) showing an increased risk. Both NOS and GRADE assessments yielded mostly low to very low-quality results.ConclusionsThis review provides no clear evidence of an association between occupational exposure to benzene and the risk of male genital cancers. Subgroup analysis suggests an increased risk of prostate cancer in high-quality studies. Nevertheless, it is important to acknowledge the methodological limitations of the available studies. Further analyses including methodologically sound studies are needed to corroborate these findings.
https://doi.org/10.1002/ajim.23740

Polybrominated diphenyl ethers (PBDEs), Occupational Exposures and Thyroid Function among U.S. and Canadian Firefighters: A Cross-sectional Study,
Gould Rothberg, B. E., Caban-Martinez, A. J., Barr, D. B., Jara, M. A., Rodriguez, V., Feliciano, P. L., Santiago, K. M., Beaver, C. C., Kobetz-Kerman, E. N. and Solle, N. S., *J Occup Environ Med*, Jun 5 2025.

OBJECTIVE: Evaluate the association between serum polybrominated diphenyl ether (PBDE) levels and thyroid anatomy and function in firefighters. METHODS: 259 firefighters provided a blood sample and underwent thyroid ultrasound. Blood serum levels were tested for thyroid function tests and PBDEs -47, -85, -99, -100, -153, and -154 (ng/g lipid weight). Ultrasonography documented

structural characteristics. Bivariate associations between PBDE concentrations and demographic/occupational characteristics, thyroid function, and thyroid anatomic measures were determined using multivariable linear regression. RESULTS: A positive relationship between PBDE-47 and triiodothyronine (p = 0.02) while an inverse relationship with free thyroxine (p = 0.03) was observed. PBDE-47 was inversely associated with thyroid nodule size (p = 0.03) and nodule aggressiveness (p = 0.02). PBDE-47 was highest in western United States firefighters and lowest among sampled Canadians (p = 0.01). CONCLUSIONS: PBDE-47 may contribute to thyroid dysregulation in firefighters. PBDE-47 levels differ across North America. https://doi.org/10.1097/jom.0000000000003477

Serum Concentration of Selected Per- and Polyfluoroalkyl Substances (PFAS) by Industry and Occupational Groups Among US Adult Workers, NHANES 2005-2014,
Gu, J. a.-O., Charles, L. a.-O., Lim, C. S., Mnatsakanova, A., Anderson, S., Dzubak, L. and Mccanlies, E., no. 1097-0274 (Electronic). Am J Ind Med, 2025 Jun;68(6):531-542

PURPOSE: Per- and polyfluoroalkyl substances (PFAS) are associated with multiple health effects including pregnancy-induced hypertension and pre-eclampsia, increased serum hepatic enzymes, increased in serum lipids, decreased antibody response to vaccines, and decreased birth weight. Millions of US workers are exposed to PFAS at their workplaces. Our objective was to estimate the serum levels of the five PFAS that are most frequently detected in the US general population(perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS), perfluorodecanoic acid (PFDA), and perfluorononanoic acid (PFNA)) among US adult workers. METHODS: Participants were 4476 workers aged ≥ 20 years with PFAS analyte results available who participated in the National Health and Nutrition Examination Survey (NHANES), 2005-2014. Geometric mean serum levels of PFAS (ng/mL) were obtained across industry and occupation groups using the PFAS subsample weight in SAS-callable SUDAAN V11. RESULTS: Among 21 industry groups, the highest geometric mean PFAS levels (ng/mL) were observed in Construction (PFOS = 12.61 ng/mL, PFOA = 3.76, PFHxS = 2.10, PFNA = 1.23, and PFDA = 0.33), followed by Utilities (PFOS = 12.46), and Real Estate/Rental/Leasing (PFOS = 12.15). The lowest geometric mean PFAS levels were seen in Private Households (PFOS = 6.34, PFOA = 2.12, PFHxS=0.75, PFNA = 0.86, and PFDA = 0.25). Among 22 occupation groups, the highest geometric mean PFAS levels were observed in Life/Physical/Social Science occupations (PFOS = 13.19, PFOA = 3.54, PFHxS= 1.69, PFNA = 1.23, and PFDA = 0.33), followed by Installation/Maintenance/Repair occupations (PFOS = 12.75), and Construction/Extraction occupations (PFOS = 12.15). The lowest geometric mean PFAS levels were found in Personal Care/Service occupations (PFOS = 7.25, PFOA = 2.43, PFHxS = 1.07, PFNA = 0.94, and PFDA = 0.25). CONCLUSIONS: Some industry and occupation groups had higher geometric mean levels of PFAS in serum compared to others. Further investigation of these industries and occupations may result in a better understanding of the sources and degree of occupational exposure to PFAS. https://doi.org/10.1002/ajim.23726

Risk of preeclampsia and gestational diabetes after occupational exposure to chemicals during pregnancy-A cohort study of births in Sweden 1994-2014,
Gustavsson, P., Lissåker, C., Albin, M., Alfredsson, L., Wiebert, P., Tinnerberg, H., Grahn, K., Rylander, L. and Selander, J., Environmental Research. Volume 279, Part 1

Many women are occupationally active during pregnancy. The aim of this study was to investigate associations between exposure to chemicals during pregnancy and the risk of gestational diabetes or preeclampsia. The cohort included singleton births in Sweden between 1994 and 2014. The cohort was limited to low-educated mothers to reduce potential confounding from unidentified life-style associated factors. Information on occupation (full-time employed) at beginning of pregnancy,

demographic data, education, personal risk factors and medical diagnoses were obtained from national records. Occupational exposure to 20 chemicals/particles was assessed by a time-specific job exposure matrix (SweJEM). Relative risks (RR) were adjusted for birth year of the child and mother's age, parity, country of birth, smoking, BMI, and occupational exposure to physical strain, low decision authority, noise, and whole-body vibrations. There were 307,985 births in the cohort. The risk of preeclampsia was elevated after exposure to diesel engine exhaust (RR 1.19; 95 % CI 1.03-1.37), gasoline engine exhaust (RR 1.26; 1.05-1.52) or to carbon monoxide (RR 1.21; 1.03-1.42). Exposure to lead was associated with an elevated risk of gestational diabetes, (RR 2.41; 1.05-5.55), based on six cases only, though. An elevated risk of preeclampsia in association with combustion products is corroborated by studies of traffic-related urban air pollution and of smoke from wildfires. Exposure to motor exhaust during pregnancy should be minimised. Exposure to lead during pregnancy should be avoided also because of serious neurodevelopmental effects for the child. https://doi.org/10.1016/j.envres.2025.121802

A Critical Review of Populations with Occupational Exposure to Per- and Polyfluoroalkyl Substances: External Exposome, Internal Exposure Levels, and Health Effects,
He, A., Liang, Y. a.-O., Li, J., Zhou, Z., Li, F., Li, Z., Wang, Y. a.-O. and Jiang, G. a.-O., Environ Sci Technol. . 2025 Jun 10;59(22):10715-10733.

The relationship between per- and polyfluoroalkyl substances (PFAS) exposure and human health has received widespread attention. This review focuses on the key distinctions in PFAS exposure between the occupational population and the general population from different countries. A systematic summary is made from the external exposure environment, exposure pathways, internal exposure levels, and health effects of the occupational population. The manufacturing, use, and disposal processes of PFAS increase their concentration levels in the ambient environment, leading to significantly higher concentrations than background areas. Different PFAS exposure pathways may lead to different molecular initiating events and health outcomes in the occupational population and the general population. Moreover, the PFAS exposure levels of the occupational population are nearly one hundred times higher than those of the general population. Mixed exposure to more unknown PFAS is another important feature of the occupational population. Although occupational exposure to PFAS is not associated with mortality, PFAS exposure can significantly disrupt metabolic pathways and cause adverse effects on the liver, kidney, and lipid homeostasis. Therefore, more stringent occupational protections for the PFAS occupational population are necessary to reduce their health risks. FAU - He, Anen
https://doi.org/10.1021/acs.est.4c14478

Evaluation of pesticide health risks and its associated metabolic health Status among nursery operators in Peninsular Malaysia,
How, V., Muhamad, S. N., Abdullah, R., Yu Bin, H. and Waras, M. N., Arch Environ Occup Health . 2025;80(7-8):175-186.

This study assessed the correlation between pesticide exposure and metabolic health among 48 nursery operators from conventional and organic farms in Peninsular Malaysia. Statistical analyses included independent t-tests and Mann-Whitney U-tests to compare group differences between conventional and organic operators, while multiple linear regression models were used to examine the correlation between pesticide exposure and health risk indicators. The results revealed that conventional nursery operators showed higher levels of metabolic health indicators, coupled with impaired liver and kidney function compared to organic operators. Significantly lower blood cholinesterase levels were observed among conventional operators, indicating a higher risk of neurotoxicity. The study highlights the substantial health hazards that nursery operators face due to

pesticide exposure, especially in conventional farming. It supports the implementation of stronger protective measures, frequent health monitoring, and a transition to safer and more sustainable nursery practices. FAU - How, Vivien https://doi.org/10.1080/19338244.2025.2522780

High serum perfluorooctanoic acid (PFOA) concentrations and interstitial lung disease in former and current workers in a fluorochemical company.
Kanetani, K., Nakamura, K., Harada, K. H., Akihisa, H., Oshima, T., Ogata, H. and Koizumi, A., Ind Health. 2025 Apr 22.

In 2002, Daikin Industries' Yodogawa Plant (DIYP) in Settsu City in Japan had contaminated drinking water in Hanshin area with perfluorooctanoic acid (PFOA), leading to the complete cessation of PFOA production in 2012. In 2023, local residents conducted a voluntary Blood Monitoring Campaign with 1,182 general residents. Blood monitoring was also conducted for former or current workers from DIYP and farming residents in Settsu City. Serum PFOA concentrations determined by gas chromatography with mass spectrometry [number: ng/mL: median (25th-75th percentile)] were as follows: former and current workers [N=7: 192.6 (23.3-596.6)] > farming residents [N=5: 70.2 (50.4-98.8] > general residents [N=1,182: 5.0 (3.3-7.0)] with significant differences (Kruskal-Wallis test, p<0.001). In a study, 4 out of 5 farming residents showed a serum PFOA decline (half-life: 2.2 yr, 95% CI: 1.4-4.6) after stopping local agricultural product consumption. However, 3 former workers exhibited no decrease over 0.8-0.9 yr. An investigation found that 5 of the 7 subjects were likely exposed to dust from the polymerization of tetrafluoroethylene or handling its particulate matters, with 3 showing Interstitial Lung Disease (ILD) signs. This suggests PFOA-laden dust may delay excretion and contribute to ILD, though the mechanistic link remains unclear, requiring further research. FAU - Kanetani, Kunio https://doi.org/10.2486/indhealth.2025-0009

Impact of Industrial Pollution on Human Renal Function and Male Reproductive Hormones: An Investigation of Heavy Metals Toxicity and Oxidative Stress,
Khdr, A. H. and Abdoulrahman, K., *Journal of Applied Toxicology*, 2025.

Industrial pollution provides significant public health risks through exposure to heavy metals (HMs). This study assessed serum HMs (Cd, Cr, Ni, Sn, Zn, and B), oxidative stress (OS) markers, renal function biomarkers, and male reproductive hormones in 135 participants across rural, urban, and industrial areas (Erbil Province, Iraq), using ICP-MS, ELISA, and automated immunoassays. Industrial workers showed significantly elevated HMs concentration, particularly for Cd [industrial: 0.203 (0.37), 95% CI: 0.136-0.288 vs. rural: 0.102 (0.07) mu g/L, 95% CI: 0.085-0.102; d = 1.2445, p = 0.007]. Conversely, Zn concentration was significantly reduced in urban [2162 (1944) vs. 3991 (1110) mu g/L in rural; d = 1.029, p = 0.0029]. OS markers (NO, CAT, and GPx) were significantly diminished in the urban/industrial areas (p < 0.0001). Whereas, 8-OHdG showed no significant differences (p > 0.05). Renal function biomarkers indicated that residents and workers in urban/industrial areas had urea increased by 26%-27%, with creatinine elevated by 16%-19% compared to the rural residents. Moreover, industrial workers had significantly higher levels of FSH, LH, and testosterone by 38.9%, 42.9%, and 24.9%, respectively, compared to the rural residents. Zn had positive associations with GPx (r = 0.6199, p < 0.0001) and CAT (r = 0.4800, p < 0.0001). Similarly, there were positive associations of Cd with creatinine (r = 0.3586, p = 0.0015) and testosterone (r = 0.3050, p = 0.0063), while it was negatively associated with CAT (r = -0.3344, p = 0.005). These findings demonstrate that HMs exposure in the industrial area causes systematic toxicity, particularly with Cd leading to renal and endocrine dysfunction by increasing OS markers. The identified exposure response associations underscore the necessity for intensive environmental monitoring and occupational safety intervention in the high-risk industrial areas.
https://doi.org/10.1002/jat.4850

HBM4EU e-waste study - Occupational exposure assessment to chromium, cadmium, mercury and lead during e-waste recycling,
Leese, E., Verdonck, J., Porras, S. P., Airaksinen, J., Duca, R. C., Galea, K. S., Godderis, L., Janasik, B., Mahiout, S., Martins, C., Mārtiņsone, I., Ani, M. M., Van Nieuwenhuyse, A., Scheepers, P. T. J., Silva, M. J., Viegas, S. and Santonen, T., *Environ Res*, Oct 15 2025, Vol. 283, p. 121892.

Processing of electronic waste (e-waste) causes the release of toxic substances which may lead to occupational exposure. The study aimed to gather information on potential occupational exposure during e-waste recycling, with a focus on biomonitoring of chromium, cadmium, mercury and lead. In eight European countries, 195 workers involved in the recycling of lead batteries, white goods, brown goods and metals and plastics were studied. These workers were compared to 73 controls with no direct involvement of e-waste recycling or other metal processing activities. The samples collected consisted of urine, blood and hair samples, along with personal air samples, hand wipes, settled dust samples and contextual information. Chromium, cadmium, mercury and lead was measured in urine, hair, air samples, hand wipes and settled dust; cadmium and lead in whole blood and chromium in red blood cells. Results showed that lead exposure is of concern, with workers from all five types of e-waste showing exposure, with elevated measurements in all matrices. Internal exposure markers were positively correlated with markers of external exposure, indicating workers are not adequately protected. Exposure to mercury and cadmium was also observed but to a much lesser extent with raised cadmium concentrations in urine and blood of all workers when compared to controls and raised mercury concentrations were found in brown goods workers when compared to controls. This study has highlighted exposure concerns when processing e-waste, particularly for lead across all waste categories studied, indicating a need for improved control measures in this sector. https://doi.org/10.1016/j.envres.2025.121892

Exploratory research on occupational exposures and breast cancer risk in the CECILE study,
Leung, L. a.-O., Koushik, A. a.-O., Cordina-Duverger, E. a.-O., Siemiatycki, J. a.-O. and Guénel, P. a.-O. X., Occup Environ Med. 2025 May 18;82(3):139-147.

OBJECTIVES: In 'exploratory mode', to examine associations between occupational exposure to 49 prevalent agents and breast cancer risk. METHODS: In a French population-based case-control study on breast cancer (2005-2007), lifetime occupational histories of 1230 incident cases and 1315 controls were collected. An industrial hygienist coded each job held by a participant. Job codes were subsequently linked to the Canadian job-exposure matrix, and exposure level estimates for numerous agents were generated. Multivariable unconditional logistic regression was used to estimate associations between occupational exposure to 49 prevalent agents and breast cancer risk, adjusting for established breast cancer risk factors and selected sociodemographic covariates. RESULTS: Increased ORs, ranging between 1.33 and 2.39, were observed for women in the highest tertile of cumulative exposure versus unexposed for the following 12 agents: sodium carbonate, synthetic fibres, wool fibres, silk fibres, organic dyes and pigments, plastic dusts, plastics pyrolysis fumes, ozone, nitrogen oxides, anaesthetic gases, aliphatic ketones and mononuclear aromatic hydrocarbons. When stratified by menopausal status, the ORs for many of these agents were stronger among premenopausal versus postmenopausal women. CONCLUSIONS: These findings suggest the possible role of some occupational agents in the aetiology of breast cancer. Further studies, based on large sample sizes and high-quality exposure assessment, are needed to confirm our findings. https://doi.org/10.1136/oemed-2024-110021

Association between size-resolved PM(10)-bound heavy metal and metalloid exposure and oxidative stress among waste recycling workers,

Li, X. and Guo, Y., *Sci Rep*, Jul 16 2025, Vol. 15, no. 1, p. 25785.

Following the sharp increase in global waste generation, heavy metals and metalloids (HMMs) have become a serious threat to workers in the waste recycling industry. However, our understanding of internal exposure levels of HMMs and the relationship between size-resolved particulate matter (PM)-bound HMMs external exposure with internal exposure and oxidative stress among waste recycling workers are limited. Therefore, we collected first morning void urine samples from 20 participants and size-resolved indoor PM(10) samples at least 45 consecutive days. We then detected 21 urinary HMMs, PM(10)-bound HMMs and oxidative stress biomarkers (OSBs) of DNA (8-hydroxy-2'-deoxyguanosine [8-OHdG]) and lipids [malondialdehyde (MDA)]. The intraclass correlation coefficients for most HMMs and OSBs ranged from fair to excellent. Linear mixed model analysis showed that urinary HMMs were predominantly affected by warehouse PM(1.1-2.1) and PM(3.3-4.7) HMM inhalation ($p < 0.05$). Participant 8-OHdG levels were correlated with PM(0.43-10) HMM inhalation, particularly in the ranges of PM(0.43-0.65), PM(4.7-5.8), and PM(9.0-10), with every unit increase in the ln-transformed average daily intake (ADI) generating a 4.30-28.0% increase in urinary 8-OHdG ($p < 0.05$). Furthermore, MDA levels were generally correlated with PM(0.43-2.1) HMM inhalation ($p < 0.05$), especially in the PM(0.43-0.65) range, with each unit increase in the ln-transformed ADI generating a 8.5-24.1% increase in urinary MDA. This study reveals the fair to excellent long-term reproducibility of urinary HMM and OSBs and the association between high-level PM-bound HMM exposure and early health impairment for an actual working environment. https://doi.org/10.1038/s41598-025-09250-1

The effects of parental occupational exposures on autism spectrum disorder severity and skills in cognitive and adaptive domains in children with autism spectrum disorder,
Mccanlies, E. C., Gu, J. K., Ma, C. C., Sanderson, W. T., Ludeña-Rodriguez, Y. J. and Hertz-Picciotto, I., *International Journal of Hygiene and Environmental Health*, Jul 2025, Vol. 268.
https://doi.org/10.1016/j.ijheh.2025.114613

Occupational pesticide exposure and cognitive impairment among adult farmers in northern Thailand,
Phitsadang, N., Naksen, W. and Ong-Artborirak, P., *Rocz Panstw Zakl Hig*, Jun 26 2025, Vol. 76, no. 1, p. 29-37.

BACKGROUND: Thai farmers are directly exposed to pesticides, which may result in adverse effects including cognitive impairment. OBJECTIVE: The aim of this study was to examine the association between occupational pesticide exposure and cognitive decline among adult farmers in northern Thailand. MATERIAL AND METHODS: This cross-sectional study included 303 pesticide-using farmers over the age of 50 from Doi Tao District in Chiang Mai Province. Pesticide exposure score was calculated using an algorithm that considered personal protective equipment (PPE) scores and exposure intensity scores, as well as lifetime application days. The scores were classified as high or low exposure based on their median. The Thai version of the Montreal Cognitive Assessment (MoCA) test was used to assess cognitive function. RESULTS: The mean age of adult farmers was 58.74 years. The prevalence of cognitive impairment was 93.7%, with an average score of 19.6. Spearman's rank correlation coefficient showed that the MoCA score was adversely correlated with lifetime application days ($r(s) = -0.145$), PPE score ($r(s) = -0.163$), exposure intensity score ($r(s) = -0.184$), and pesticide exposure score ($r(s) = -0.225$). Linear regression revealed that high exposed farmers had significantly lower MoCA scores than low exposed farmers, as measured by PPE score ($B = -0.75$; 95% CI: -1.46, -0.05), exposure intensity score ($B = -0.97$; 95% CI: -1.66, -0.27), and pesticide exposure score ($B = -0.77$; 95% CI: -1.47, -0.06), after controlling for sex, age, education, income sufficiency, and body mass index. CONCLUSIONS: Thai farmers are at risk of cognitive

impairment linked to occupational pesticide exposure, depending on their PPE use and exposure intensity. There is still a critical need for action to reduce the risk of negative health effects from pesticide exposure among Thai farmers. https://doi.org/10.32394/rpzh/200912

Epidemiology and occupational risk factors of male infertility based on 3,025 patients in Eastern Morocco during 2021-2023: a cohort study,
Rochdi, C., Ouadrhiri, M., Bellajdel, I., Taheri, H., Saadi, H., Mimouni, A. and Choukri, M., *Obstetrics & Gynecology Science*, May 2025, Vol. 68, no. 3, p. 198-209.

Objective The objective of our study was to characterize the sperm parameters of men consulting for infertility in our fertility center. Methods The study included 3,025 patients investigated from September 2021 to July 2023. Demographic data, infertility risk factors, and the primary or secondary nature of infertility were recorded for each patient. The sperm parameters were analyzed according to World Health Organization (WHO) criteria (2021). Results The average age of the patients was 40 years. The average duration of infertility was 5.5 years. Primary infertility was noted in 2,736 patients (88.97%). The most common risk factors for infertility were occupational exposure, followed by varicocele. Lifestyle factors associated with male infertility included smoking (24.29%), alcohol consumption (12.49%), and high temperature exposure (30.08%). Spermogram abnormalities were observed in 78.71% of cases. Spermocytogram abnormalities were found in 63.1% of cases. Sperm count, morphology, total motility, and vitality below WHO (2021) reference values were found in 25.60%, 34.13%, 32.29%, and 62.46% of the analyzed samples, respectively. Seminal fluid analysis revealed oligozoospermia in 29.07% of cases, asthenozoospermia in 24.68%, and azoospermia in 17.56%. Oligo-astheno-necrospermia was the most frequently observed combined abnormality (10.0%). Conclusion This study showed a high rate of abnormal semen quality in male partners of infertile couples. Male infertility is often multifactorial and results in quantitative and/or qualitative sperm abnormalities. https://doi.org/10.5468/ogs.24297

Per- and polyfluoroalkyl substance emission from waste thermal treatment: A review,
Safarzadeh, H., Bonato, T., Ebrahimzadeh Sarvestani, M. and Di Maria, F., *Waste Manag Res*, Jul 28 2025, p. 734242x251349211.

The objective of this study is to examine the content of per- and polyfluoroalkyl substance (PFAS) in the emissions from waste containing PFAS thermal treatment. The study is reviewed according to PRISMA 2020. Scopus, Web of Science and PubMed are the databases used. The publishing period is from 2020 to 7 August 2024; only studies written in English language are included; studies reporting on analysis of PFAS in the inlet, outlet streams and removal efficiency; combustion, oxidation, hydrothermal carbonization, pyrolysis and gasification processes; waste from full-scale facilities are considered. Two of three researchers screened the studies for eligibility. One researcher extracted the data and the other two reviewed them for accuracy. Data were then organized based on the statistical information reported in each included study. A total of 14 studies were included. From equation ∑ i = 1nPFASi, mean concentration of each PFAS(i) in the inlet waste ranged from 9.3 ng g(-1) DM to 203.9 ng g(-1) DM. PFPeA, perfluoro octane sulfonate (PFOS) and PFHxA compounds were compared with those of higher concentration in inlet waste ranging from 30 ng g(-1) wb, for PFOS, to about 400 ng g(-1) wb, for PFPeA. Removal efficiency was calculated as a mass balance among inlet and outlet of investigated PFAS, ranged from 30% to 100%. Maximum removal efficiencies were detected for process temperatures ⩾550°C and retention time ⩾2 seconds. Thermal treatment of PFAS containing waste achieves high level of PFAS removal when operated at high temperatures and proper gas residence time. More research is needed for better assessing the effective mineralization of PFAS in the outlet stream and the presence and fate of potential reactive compounds due to incomplete combustion. https://doi.org/10.1177/0734242x251349211

Evaluation of pesticide residues in greenhouse workers' blood serum using QuEChERS-UHPLC-MS/MS method and associated health risks,
Salari, E., Esmaeilian, M., Faryabi, R., Mahdavi, V., Mashayekhi-Sardoo, H. and Askarpour, H., *Food Chem Toxicol*, Sep 2025, Vol. 203, p. 115612.

Pesticide exposure in greenhouse workers poses considerable health risks, requiring continuous evaluations of pesticide residues and their potential effects on human health. This article evaluated the level of pesticide residues in greenhouse workers' sera in Jiroft County, Iran, and assessed the possible health risks. The cross-sectional study was conducted from December 20, 2023, to January 20, 2024, and involved 84 greenhouse workers. Seventy-four pesticide residues were detected using the QuEChERS-UHPLC-MS/MS method. Health risk assessments were carried out, focusing on carcinogenic and non-carcinogenic risks. The findings demonstrated that insecticides (48.4 %) and fungicides (30.3 %) were the most frequent, and diazinon was the most commonly detected pesticide. Health risk assessments revealed that exposure to emamectin benzoate and pyraclostrobin resulted in higher health risks, with emamectin benzoate indicating a non-carcinogenic risk (hazard quotient: 2.3). The carcinogenic risk findings proposed that it seems unlikely that pyraclostrobin and emamectin benzoate are carcinogenic. The humid and semi-closed conditions of greenhouses enhance the risk of pesticide exposure, affecting vulnerable populations. The study indicates the need for promoted safety protocols and training programs to reduce exposure risks. Future research should focus on longitudinal studies to evaluate the long-term health impacts of pesticide exposure and the effectiveness of intervention strategies.
https://doi.org/10.1016/j.fct.2025.115612

Epidémiologie

Dietary intake of polycyclic aromatic hydrocarbons (PAHs) and breast cancer risk: Evidence from the French E3N-Generations prospective cohort,
Amadou, A., Praud, D., Marques, C., Noh, H., Frenoy, P., Vigneron, A., Coudon, T., Deygas, F., Severi, G., Fervers, B. and Mancini, F. R., *Environment International*, Jun 2025, Vol. 200.

Background: While there is compelling evidence of the association between occupational exposure to polycyclic aromatic hydrocarbons (PAHs) and risk of breast cancer (BC), findings on PAH dietary exposure are less consistent. The present study aims to evaluate the association between PAH dietary intake and BC risk. Methods: The study included 67,879 women who completed a validated semi-quantitative dietary questionnaire (208 food items) from the E3N-Generations cohort study. PAH dietary intake was estimated by combining E3N food consumption data with food contamination levels obtained from the second French total diet study (TDS2). Cox regression was used to estimate adjusted hazard ratios (HRs) and 95 % confidence intervals (CIs) for the association between PAH dietary intake (sum of four PAHs (PAH4) namely benzo[a]pyrene (BaP), chrysene (CHR), benzo[a]anthracene (BaA) and benzo[b]fluoranthene (BbF)) and BC risk. Additionally, BaP, a surrogate for total PAHs, was investigated as the second exposure variable. Results: After an average follow-up of 17.6 years, 5,686 incident BC were diagnosed. Overall, the estimated HRs for the associations between each quintile of PAH4 and BC risk, taking the first quintile as reference, were all greater than 1, but were statistically significant only for the third quintile (HRQ3 vs Q1 = 1.10; CI: 1.01-1.20). By estrogen (ER) and progesterone (PR) hormone receptor status, we observed a positive association between PAH4 dietary intake and ER-PR- BC (HRQ4 vs Q1 = 1.34; CI: 1.01-1.76). Moreover, there was a borderline positive association with BaP, for the second (HRQ2 vs Q1 =

1.08; CI: 0.99-1.17) and third (HRQ3 vs Q1 = 1.07; CI: 0.98-1.16) quintiles. Conclusions: This study supports a relationship between PAH4 dietary intake and BC risk, notably with a nonlinear trend. A positive but marginal association was observed between BaP dietary intake and BC risk.
https://doi.org/10.1016/j.envint.2025.109505

Exposure to polyoxyethylene tallow amines (POEAs), glyphosate co-formulation surfactants, in a US pregnant population and their potential endocrine disrupting effects,
Amreen, B., Lesseur, C., Jagani, R., Yelamanchili, S., Barrett, E. S., Nguyen, R. H. N., Sathyanarayana, S., Swan, S. H., Andra, S. S. and Chen, J., *Environmental Pollution*, Jun 1 2025, Vol. 374.

Emerging but inconsistent evidence suggests that glyphosate (GLY)-based herbicides (GBHs) are more toxic than the active ingredient, GLY alone. Polyoxyethylene tallow amines (POEAs) are surfactants most widely used in GBH formulations, making up to 5-15 % by weight. However, neither POEA exposure nor their toxicity has been well studied in the general population. This study leverages second trimester urine samples collected from 86 pregnant participants of a multi-center, US-based pregnancy cohort. We measured three POEA homologs, i.e., C(16)s(EO)(2), C(18)u(EO)(2), and C(18)s(EO)(2), using an ultrahigh performance liquid chromatography-tandem with mass spectrometry. These homologs were detected in 79 %, 97 %, and 59 % of the samples (LOD: 0.1 ng/mL) at a mean concentration of 1.87, 1.88, and 1.65 ng/mL, respectively. While these homologs were highly correlated with each other (rho >0.7), their correlations with GLY and its breakdown product, aminomethylphosphonic acid (AMPA), were moderate (rho <0.4). Compared to other races, the POEA level in urine was the lowest in White participants (p = 0.047). We observed an indication that a higher POEA level was associated with increased ano-genital distance (AGD), a marker of gestational androgen milieu, in male infants only (beta = 2.46, p = 0.057); such relationship remained unchanged after adjusting for GLY (beta = 2.45, p = 0.055) or AMPA (beta = 2.46, p = 0.058). Despite the small sample size, our study provides the first population data on POEA exposure which demonstrates widespread exposure in the general population. Suggestive associations between urinary POEA and AGD in male newborns implicate potential endocrine disrupting property of POEA, which warrant further investigation in larger studies.
https://doi.org/10.1016/j.envpol.2025.126205

Association between endocrine disrupting chemicals and female infertility: a study based on NHANES database,
Bingru, L., Ting, C., Zhe, Z., Wen, J., Qianling, Z. and Hailun, Z., *Frontiers in Public Health*, Jun 30 2025, Vol. 13.

Background Controversy persists regarding the impact of endocrine disrupting chemicals (EDCs) on female infertility, and the specific EDCs that cause female infertility remain unclear. This study aims to examine the associations between various EDCs metabolites and female infertility using data from the female population in the National Health and Nutrition Examination Survey (NHANES) conducted between 2001 and 2006.Methods A cross-sectional study on reproductive-age women aged 18-45 years was conducted, with data retrieved from the NHANES database. Multivariate logistic regression analysis was performed to evaluate the association between EDCs metabolites and female infertility. Subgroup analysis was applied to stratify by age and body mass index (BMI). Results were summarized using an odds ratio (OR) with a 95% confidence interval (CI).Results A total of 3,982 women were enrolled, comprising 463 infertile women and 3,519 control women. The results showed that increased exposure to EDCs metabolites (including DnBP, DEHP, DiNP, DEHTP, PAEs, Equol, PFOA, and PFUA) was significantly associated with female infertility, with odds ratios of 2.10 (95% CI: 1.59, 2.48), 1.36 (95% CI: 1.05, 1.79), 1.62 (CI: 1.31, 1.97), 1.43 (95% CI: 1.22, 1.78), 1.43 (95% CI: 1.26, 1.75), 1.41 (95% CI: 1.17, 2.35), 1.34 (95% CI: 1.15, 2.67), and 1.58 (95% CI: 1.08,

2.03), respectively. Sensitivity analyses confirmed the robustness of these findings. The subgroup analysis also indicated that increased age and BMI may exacerbate the risk of female infertility among those exposed to EDCs metabolites.Conclusions This study indicates that exposure to EDCs metabolites such as PAEs, equol, and PFASs are associated with female infertility. These findings provide valuable evidence for preventing female infertility from the perspective of EDCs exposure. https://doi.org/10.3389/fpubh.2025.1608861

Periconception bisphenol and phthalate concentrations in women and men, time to pregnancy, and risk of miscarriage,
Blaauwendraad, S. M., Boxem, A. J., Gaillard, R., Kahn, L. G., Lakuleswaran, M., Sakhi, A. K., Bekkers, E. L., Mo, Z. X., Spadacini, L., Thomsen, C., Steegers, E. a. P., Mulders, A., Jaddoe, V. W. V. and Trasande, L., *Environmental Research*, Aug 1 2025, Vol. 278.

Background: Exposure to endocrine-disrupting chemicals such as bisphenols and phthalates might lead to adverse fertility and early pregnancy outcomes. Methods: This study was embedded in the Generation R Next Study, a population-based cohort study from preconception onwards. Urinary phthalate and bisphenol concentrations were assessed in the preconception period (938 women), defined as the period in which couples were actively trying to conceive, and early pregnancy (1,366 women and 1,202 men, mean gestational age at sampling 86 weeks). Time to pregnancy and miscarriage were assessed using questionnaires and ultrasounds. Subfertility was defined as the inability to conceive within 12 months or need for assisted reproductive technologies. Findings: Higher preconception urinary bisphenol S (BPS) and cyclohexane-1,2-dicarboxylic acid-monocarboxy isooctyl ester (mCOCH) concentrations in women were associated with longer time to pregnancy. Higher preconception mono-[(2-carboxymethyl)hexyl] phthalate, mono-2-ethyl-5-oxohexyl phthalate (mEOHP), mono-(7-carboxy-n-heptyl)phthalate (mCHpP), and mono benzyl phthalate (mBzBP) were associated with shorter time to pregnancy, and higher mono-2-ethyl-5-hydroxyhexyl phthalate (mEHHP), mEOHP, and mBzBP with lower odds of subfertility. In men, higher early pregnancy BPS, mCHpP, mono-4-methyl-7-hydroxyoctyl phthalate, mono-4-methyl-7-oxooctyl phthalate, and mono-ethyl phthalate were associated with shorter time to pregnancy or lower odds of subfertility. Higher preconception or early pregnancy BPS, phthalic acid, and mCHpP in women were associated with lower odds of miscarriage, whereas higher mono-carboxy-isoctyl phthalate, mCOCH, and mono-2-(propyl-6-carboxy-hexyl)-phthalate (cxmPHxP) with higher odds of miscarriage (all p-values <005). Interpretation: Preconception and early pregnancy exposure to bisphenols and phthalates may affect couple fertility. Our results should be considered as hypothesis generating and replicated in future studies, possibly including repeated chemical measurements and mixture analysis. https://doi.org/10.1016/j.envres.2025.121712

Phthalates and bisphenols early-life exposure, and childhood allergic conditions: a pooled analysis of cohort studies,
Boissiere-O'neill, T., Lazarevic, N., Sly, P. D., Ponsonby, A. L., Chen, A. M., Azad, M. B., Braun, J. M., Brook, J. R., Burgner, D., Lanphear, B. P., Moraes, T. J., Saffery, R., Subbarao, P., Turvey, S. E., Yolton, K., Vilcins, D., Grp, C. I. and Grp, B. I. S. I., *Journal of Exposure Science and Environmental Epidemiology*, 2025.

BackgroundExposure to plastic additives, such as phthalates and bisphenols, has been associated with a higher risk of allergic conditions, but the evidence is inconsistent for children younger than five.ObjectiveTo examine the association between pre- and postnatal urinary phthalates and bisphenols, and allergic conditions, and potential effect modification by sex, in pre-school children, through a pooled analysis.MethodsWe pooled data from the Barwon Infant Study (Australia), the Canadian Healthy Infant Longitudinal Development Study (Canada), the Health Outcomes and

Measures of the Environment (United States) and the Environmental Influences on Child Health Outcomes-wide cohorts (United States). Urinary phthalates and bisphenols were measured during pregnancy and early childhood. We estimated daily intakes from urinary concentrations, except for mono-(3-carboxypropyl) phthalate (MCPP). Outcomes, including asthma, wheeze, eczema, and rhinitis, were assessed up to five years of age through questionnaires and clinical assessments. We used generalised estimating equations for single compounds and quantile G-computation for the chemical mixtures.Results5306 children were included. A two-fold increase in prenatal dibutyl phthalates (DBP; risk ratio [RR] = 1.08; 95% confidence interval [CI]: 1.00-1.16) and benzyl butyl phthalate (BBzP; RR = 1.06; 95%CI: 1.00-1.12) increased the risk of asthma in children under five. Prenatal MCPP levels were associated with rhinitis (RR = 1.05; 95%CI: 1.01-1.09). Postnatal BBzP levels increased the risk of wheezing (RR = 1.05; 95%CI 1.01-1.09), as well as di(2-ethylhexyl) phthalate (DEHP; RR = 1.06; 95%CI: 1.01-1.11) and MCPP (RR = 1.09; 95%CI: 1.04-1.14). These were also inversely associated with eczema. A one-quartile increase in the postnatal chemical mixture increased the risk of wheezing (RR = 1.14; 95%CI: 1.02-1.26). There was limited evidence of effect modification by sex.ImpactPhthalates and bisphenols are widespread and may contribute to allergic conditions in children. We pooled data from 5000 children across multiple birth cohorts, suggesting that early-life exposure to these chemicals is associated with increased risks of asthma, wheezing, and rhinitis by age five. We further investigated the timing of exposure, non-linear dose-response relationships, and effect measure modification by sex. This study provides a comprehensive assessment of early-life exposure to phthalates and bisphenols and strengthens the evidence for their role in the development of childhood allergic outcomes. https://doi.org/10.1038/s41370-025-00790-2

Associations between environmental chemical mixtures and anthropometric measures in Korean girls: a cross-sectional study,
Bolormaa, E., Kim, K., Jhang, H., Cho, Y. M., Enkhbat, U. and Choe, S. A., *European Journal of Pediatrics*, Jun 16 2025, Vol. 184, no. 7.

The purpose of this study is to investigate the association between environmental chemicals and anthropometric indices using preliminary data from the Puberty and Environment in Adolescents Cohort Project. Random urine samples from 370 Korean girls aged 7-14 years were evaluated for 15 environmental phthalates, phenols, polycyclic aromatic hydrocarbon metabolites, and three heavy metals using growth metrics. We calculated the body mass index (BMI) z-score, weight z-score, height z-score, and waist-to-hip ratio (WHR) based on the World Health Organization growth references. Associations between environmental chemicals and weight and height indicators were assessed using single- and mixture-exposure models, controlling for the measured covariates. We identified 28 girls (7.6%) as overweight, 10 (2.7%) as underweight based on BMI z-scores, 17 (4.6%) as underweight based on weight z-scores, and 6 (1.6%) as having a low height status. Normal anthropometric measurements were reported in 85.9% of the girls. No positive associations between environmental chemical mixtures and BMI z-score, weight z-score, or WHR (beta = -0.03, 95% confidence interval [CI]: -0.34, 0.26; -0.23, 95% CI: -0.51, 0.06; -0.00, 95% CI: -0.02, 0.02) were observed. A negative association was identified between environmental phthalate, phenol, and polycyclic aromatic hydrocarbons metabolites, and height z-score (beta = -0.41, 95% CI: -0.63, -0.19). Heavy metal mixtures were negatively associated with weight and height z-scores (beta = -0.20, 95% CI: -0.37 to -0.04; -0.21, 95% CI: -0.40 to -0.03).Conclusion: Exposure to environmental chemical mixtures was negatively associated with height in girls. The different patterns of association observed in the single and mixture analyses provide insights into the health impacts of multiple chemicals on children. What is Known:center dot Environmental chemical mixtures including phenols, phthalates, PAHs, and heavy metals are associated with abnormal growth in children. center dot Exposure to these mixtures may influence body mass index and other

anthropometric measures throughout childhood.What is New:center dot This study evaluated the effects of environmental chemical mixtures on anthropometric indices in Korean adolescent girls, using a mixture-exposure approach.center dot Exposure to phthalates, phenols, polycyclic aromatic hydrocarbons, and heavy metals was inversely associated with height, whereas associations with body mass index, weight, or waist-to-hip ratio were not observed. https://doi.org/10.1007/s00431-025-06255-w

Mixtures of chemicals in pregnancy and their effects on cognitive and fine motor abilities in childhood,
Brennan Kearns, P., González, L., Soler-Blasco, R., Andiarena, A., Santa-Marina, L., Casas, M., Burgaleta, M., Vrijheid, M. and Guxens, M., *Environ Res*, Jul 19 2025, Vol. 285, no. Pt 2, p. 122380.

This study evaluates effects of a mixture of 29 chemicals in pregnancy (organochlorine compounds, per - and polyfluoroalkyl substances, phenols, and phthalates) on cognitive abilities (working memory, attentional function, visuomotor attention, cognitive flexibility, verbal and non-verbal intelligence, information processing speed, risky decision making) and fine motor function in childhood. Data from over 2000 mothers and their children that take part in the INfancia y Medio Ambiente in Spain were analyzed. Quantile-based g-computation estimated joint effects of chemical mixtures on the outcomes, adjusting for confounders and using inverse probability weights to mitigate selection bias. The overall mixture of chemicals was linked to lower visuomotor attention (i.e., slower response time, +0.2 min, 95 % CI 0.0 to 0.4 for the second; +0.4 min, 95 % CI 0.0 to 0.8 for the third; and +0.7 min, 95 % CI 0.0 to 1.3 for the fourth quartile, relative to the first quartile). Counterintuitively, the overall mixture of chemicals was related to higher verbal intelligence (+1.5 points, 95 % CI 0.1 to 3.0 for the second; +3.0 points, 95 % CI 0.1 to 6.0 for the third; and +4.6 points, 95 % CI 0.2 to 9.0 for the fourth quartile, relative to the first quartile). However, neither of these associations survived multiple testing correction. Our study does not provide strong evidence that prenatal exposure to a mixture of organochlorine compounds, per - and polyfluoroalkyl substances, phenols, and phthalates affects cognitive abilities or fine motor function in childhood. https://doi.org/10.1016/j.envres.2025.122380

Endocrine disrupting chemicals exposure and health: An umbrella review,
Chen, J. H., Song, P., Li, C., Liu, H. J., Zhang, L., Zhou, Y., Zhou, Z. and Yan, W. G., *Ecotoxicology and Environmental Safety*, Sep 1 2025, Vol. 302.

The aim of this umbrella review was to evaluate the quality, potential biases, and validity of the existing evidence on the relationship between endocrine disrupting chemicals (EDCs) exposure and health outcomes, through a comprehensive review of available meta-analyses. The included meta-analyses were searched across multiple databases, including PubMed, Embase, and Web of Science. This umbrella review included systematic reviews and meta-analyses of randomized controlled trials, cohort studies, case-control studies, and cross-sectional studies that assessed the impact of EDCs exposure on various health outcomes in humans. The search resulted in the identification of 67 meta-analyses and 109 health outcomes from 7552 unique articles. All of these 109 health outcomes were derived from meta-analyses of observational studies. EDCs exposure included pesticides (n = 30), BPA (n = 13), PAHs (n = 18), PFAS (n = 10), and heavy metals (n = 38). Sixty-nine harmful associations were found to be statistically significant, along with one beneficial association. The remaining 39 outcomes were either harmful or beneficial but did not reach statistical significance. Significant harmful associations between EDCs exposure and 22 cancer outcomes, 21 neonatal/infant/child-related outcomes, 18 metabolic disorder outcomes, 17 cardiovascular disease outcomes, 11 pregnancy-related outcomes, and 20 other outcomes (renal, neuropsychiatric, respiratory, and hematologic) were detected. Exposure to environmental EDCs is closely linked to a

wide range of adverse health outcomes. Given the widespread exposure to these pollutants globally, precautionary policies may be warranted to reduce population-level exposure and mitigate potential health risks associated with environmental chemicals.
https://doi.org/10.1016/j.ecoenv.2025.118574

Association between per- and polyfluoroalkyl substances and unexplained recurrent spontaneous abortion: A case-control study in China,
Cheng, Q., Lv, C., Li, Y., Song, H., Li, S., Li, D., Han, Y., Zhao, F. and Lin, Q., *Ecotoxicology and Environmental Safety*, 2025/08/01/ 2025, Vol. 301, p. 118496.

Although prior studies have identified that per- and polyfluoroalkyl substances (PFASs) were associated with adverse pregnancy outcomes, the potential influence of PFASs exposure on unexplained recurrent spontaneous abortion (URSA) remains uncertain. Our case-control study aimed to explore the associations between PFASs and URSA, including 110 URSA cases and 91 controls from Beijing. Concentrations of 15 PFASs in serum were measured using ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS). The associations between PFASs and the risk of URSA were then analyzed using multiple logistic regression. Compared to the lowest tertile, PFBA (2nd (OR: 4.26; 95 % CI: 1.92, 9.45), 3rd (OR: 8.10; 95 % CI: 3.48, 18.89)), PFDoDA (2nd (OR: 2.17; 95 % CI: 1.72, 4.35), 3rd (OR: 3.18; 95 % CI: 2.24, 4.85)), PFHxS (3rd (OR: 2.46; 95 % CI: 1.15, 5.25) and PFHpS (3rd (OR: 2.56; 95 % CI: 1.15, 5.69) were positively associated with higher risks of URSA. 6:2 Cl-PFESA was significantly associated with decreased risks of URSA. Weighted quantile sum (WQS) regression analyses, Quantile g-computation (QGC) and Bayesian kernel machine regression (BKMR) identified PFBA and PFDoDA as the primary contributors to the mixed effects of PFASs on URSA. We found that maternal serum PFASs, especially PFBA and PFDoDA may increase the risk of URSA.
https://doi.org/https://doi.org/10.1016/j.ecoenv.2025.118496

Early-life exposure to organophosphate esters and child neurodevelopment in the French national birth cohort,
Chupeau, Z., Mercier, F., Bot, B. L., Siméon, T., Chauvet, G., Bonvallot, N., Zaros, C., Charles, M. A., Glorennec, P. and Chevrier, C., Environment International Volume 200, June 2025

Organophosphate esters (OPEs) are ubiquitous flame retardants and/or plasticizers, raising concerns regarding their possible neurodevelopmental toxicity. We aimed to explore association between pre- and post-natal exposure to OPEs and cognitive abilities among 3.5-year-old children. We included 381 mother-child pairs from the French ELFE national birth cohort. Pre- and post-natal exposures were estimated using concentrations of 9 OPEs measured in the hair of mothers collected at birth and children at age 3.5. Children's cognitive development was evaluated using the Picture Similarities Test (PST) from the British Ability Scale. Analyses were weighted in order to transpose results to French births in 2011. For each OPE, the association with PST scores was assessed by linear regression accounting for DAG-selected adjustment covariables. The only observed association between prenatal exposure to OPEs and PST score was a decrease of 4.5 points (95 %CI: -8.8, -0.3) among the 25 % of mothers having the highest hair-concentrations of tri-n-butyl phosphate (TBP) versus the 25 % having the lowest ones. Regarding childhood exposure, we observed a decrease (-1.9 points, 95 %CI: -3.0, -0.8) in PST score per twofold increase in children's hair-concentrations of ethylhexyl diphenyl phosphate (EHDPP). Decreased scores were also observed for higher childhood exposure levels for triphenyl phosphate (TPHP). An increase in the PST score was observed for the intermediate category of childhood exposure levels for tris(2-chloropropyl) phosphate (TCPP). While no adverse associations were observed for several OPEs,

neurodevelopmental health concerns were raised in the present study for three ubiquitous OPEs, TBP, TPHP and EHDPP. https://doi.org/10.1016/j.envint.2025.109558

Phenol biomarker concentrations in human ovarian follicular fluid and the associations with in-vitro fertilization outcomes,
Dimitriadis, I., Souter, I., Williams, P. L., Weller, D., Ford, J. B., Hauser, R. and Mínguez-Alarcón, L., *International Journal of Hygiene and Environmental Health*, Jul 2025, Vol. 268.

Background: Phenols are a family of short-lived endocrine disrupting chemicals found in a wide range of products and have drawn significant attention because of widespread human exposure and their potential adverse effects on reproductive health. Phenols have been widely detected in several human bodily fluids, particularly in urine and blood. However, there is limited data on phenols in human ovarian follicular fluid (FF). In addition, studies suggest associations between exposure to bisphenols and measures of infertility in humans. Nevertheless, the association of FF concentrations of bisphenols and female fertility has not been investigated. Objectives: To quantify phenols in human ovarian FF, investigate correlations of phenol concentrations between FF and urine, evaluate trends over time, and explore any associations between FF concentrations of phenols and in-vitro fertilization (IVF) outcomes. Methods: This analysis includes 143 women who enrolled in the Environment and Reproductive Health (EARTH) Study and underwent one IVF cycle between 2009 and 2015, with available, FF, urine and reproductive outcome data. FF concentrations of 2,4-dichloro-phenol (2,4DCP), 2,5-dichloro-phenol (2,5DCP), methyl-paraben (MPB), ethyl-paraben (EPB), propyl-paraben (PPB), butyl-paraben (BPB), bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), benzophenone-3 (BP3), triclosan (TCS) and triclorocarban (TCC) were quantified by isotope dilution tandem mass spectrometry. Generalized linear models were used to explore the associations between FF concentrations of bisphenols (in tertiles or dichotomized) and IVF outcomes, adjusting for confounders. Results: Detection rates varied from high (79-95 %) for MPB, PPB and BPS, to moderate (44-65 %) for BPA, BP3 and TCS, to low (1-34 %) for 2,4DCP, 2,5DCP, EPB, BPB, BPF, TCC. Correlations between FF and urine were strong for BP3 (r = 0.86), moderate for MPB (r = 0.64) and PBP (r = 0.63), and weak for BPS (r = 0.21) and BPA (r = 0.12). FF BPA concentrations significantly decreased over time, whereas FF BPS concentrations increased. Most of the examined FF phenol biomarker concentrations were not related to early IVF outcomes (endometrial thickness, total and mature (MII) oocyte yield, fertilization rates). However, significant associations between PPB and endometrial thickness, and between BP3 and MII oocyte yield were noted, without these findings translating in any effects observed on pregnancy outcomes (implantation, clinical pregnancy and live birth). Conclusions: We observed that most phenols were detected in FF and there were some correlations with urinary concentrations. We confirmed in FF that phenols such as BPA may be declining, while exposure to new replacements such as BPS are increasing. However, no overall associations were observed for the examined FF phenol biomarker concentrations with early IVF outcomes and pregnancy outcomes. Further research is needed to examine the potential associations of these phenols in FF, especially the newer ones that are on the rise.
https://doi.org/10.1016/j.ijheh.2025.114617

Co-exposure of phthalates, bisphenols, parabens, and polycyclic aromatic hydrocarbons in follicular fluid of women undergoing assisted reproductive technologies and the associations with hormone levels,
Dou, X. Y., Li, X. L., Huang, S. Y., Long, C. Y., Chen, C. R., Chen, X. and Yu, Y. X., *Journal of Environmental Exposure Assessment*, Jun 2025, Vol. 4, no. 2.

Endocrine-disrupting chemicals (EDCs), particularly phthalates (PAEs), bisphenols, parabens, and polycyclic aromatic hydrocarbons (PAHs), constitute pervasive environmental contaminants with

demonstrated potential to adversely affect female reproductive health. Although these compounds are known to exert adverse effects, critical knowledge gaps persist concerning their specific associations with reproductive outcomes. The present study analyzed 144 follicular fluid samples from women undergoing assisted reproductive technology procedures, quantifying concentrations of PAE metabolites (mPAEs), bisphenols, parabens, and hydroxylated PAHs (OH-PAHs). Analytical results demonstrated a descending concentration gradient: mPAEs exhibited the highest median concentration (6.14 ng/mL), followed by parabens (2.17 ng/m L), bisphenols (1.33 ng/mL), and OH-PAHs (0.26 ng/mL). Notably, the study identified a positive correlation between follicular fluid bisphenol concentrations and testosterone levels, along with a potential association between PAE exposure and elevated risk of secondary infertility. Application of Bayesian kernel machine regression and Quantile g-computation models revealed that EDCs predominantly influence hormone levels through mixture effects, with increasing chemical mixture concentrations corresponding to decreased estradiol levels on hCG trigger day and reduced basal progesterone. The models specifically identified bisphenol S (BPS) and bisphenol P (BPP) as the predominant mediators of these endocrine disruptions, respectively, suggesting that bisphenols may disrupt female reproductive health through endocrine interference mechanisms.
https://doi.org/10.20517/jeea.2025.07

Hair as an Indicator of Prolonged Paraben Exposure and Its Relation to Weight Gain in a Sample of Spanish Children: A Proof-of-Concept Study,
Gálvez-Ontiveros, Y., González-Palacios, P., Ramírez, V., Monteagudo, C., Samaniego-Sánchez, C., Rivas, A. and Zafra-Gómez, A., *Nutrients*, May 6 2025, Vol. 17, no. 9.

Background: Childhood obesity has become a major public health concern worldwide, and increasing attention is being paid to the potential role of endocrine-disrupting chemicals such as parabens. Understanding environmental contributors is essential for early prevention strategies. Objectives: The aim of the present research was to determine the presence of parabens in hair samples and to examine its association with excess weight and obesity in a sample of Spanish schoolchildren. Methods: A total of 104 cases and 166 controls (3-12 year olds) were recruited. Sociodemographic and lifestyle data and hair and urine samples were gathered. UHPLC-MS/MS coupled to a triple quadrupole detector was used for the quantitative determination of six parabens (methylparaben [MetPB], ethylparaben [EthPB], butylparaben [ButPB], propylparaben [PropPB], and isopropylparaben [i-PropPB]). The relationship between the concentration of parabens in hair and urine was examined according to Spearman correlation coefficients. Finally, binary logistic regression models were constructed to evaluate the relationship of parabens with excess weight/obesity. Results: Detected paraben levels were higher in cases. A weak correlation was produced between hair and urine concentrations, with the exception of i-PropP (hair)/PropPB (urine) and i-PropP (hair)/i-PropPB (urine) in boys, and i-PropPB (hair)/PropPB (urine) in girls. A high level of PropPB was associated with a 4.67 times greater risk of excess weight/obesity only in the boys. Conclusions: In males, a high concentration of PropPB in hair is associated with excess weight and obesity. https://doi.org/10.3390/nu17091593

Association of Organochlorine Pesticide Exposure as Endocrine Disruptors with Polycystic Ovarian Syndrome in North India,
Garg, R., Goswami, B., Singh, K., Singh, S., Agrawal, P., Gupta, P. and Verma, U., *Journal of Mid-Life Health*, Apr-Jun 2025, Vol. 16, no. 2, p. 201-207.

Aim and Background: This study explores the correlation of blood levels of organochlorine pesticides (OCPs) between PCOS and non-PCOS women, considering the endocrine-disrupting properties of OCPs and their potential role in PCOS pathogenesis. Materials and Methods: A case-control study

was conducted at Sarojini Naidu Medical College, Agra, from September 2022 to March 2024. Serum samples from 110 women diagnosed with PCOS and 110 age- and weight-matched controls were analyzed for 17 degrees CP residues using gas chromatography. Clinical examination to calculate height, weight, body mass index, and waist-hip ratio was conducted. Signs of hyperandrogenism, such as acne and hirsutism, along with acanthosis nigricans, were documented. Hormonal profiles through chemiluminescence immunoassay were assessed. Correlation analysis entails examining connections between OCP and polycystic ovarian syndrome (PCOS) through the application of the Pearson correlation coefficient. Results: PCOS patients exhibited significantly higher levels of several OCPs, including Alpha BHC, Beta BHC, Gamma BHC, Delta BHC, Heptachlor, Heptachlor Epoxide, Endosulfan I, Endosulfan II, Endosulfan Sulfate, Aldrin, Endrin, Endrin Aldehyde, PP-DDE, PP-DDT, and PP-DDD ($P < 0.05$) in comparison to their age- and weight-matched controls. Dieldrin levels showed no significant difference in both cohorts. Elevated OCP levels correlated with increased androgens, insulin resistance, menstrual irregularities, and disrupted gonadotropin secretion in PCOS patients while no association was measured in controls. Conclusion: The findings suggest that environmental exposure to OCPs is associated with PCOS exacerbates the disease by disrupting hormonal balance and acting as endocrine disruptors. Further research is needed to confirm these associations and inform targeted interventions. Clinical Significance: This study highlights the potential role of OCPs in association with PCOS, emphasizing the need for public health measures to reduce exposure to these harmful chemicals, which may help manage PCOS symptoms and improve health outcomes for affected women.
https://doi.org/10.4103/jmh.jmh_50_25

Prenatal exposures to persistent organic pollutants and menstrual characteristics in girls at age 12 in the French PELAGIE cohort,
Génard-Walton, M., Angot, E., Warembourg, C., Monfort, C., Rouget, F., Costet, N., Tillault, H., Lainé, F., Gaudreau, É., Cordier, S., Kvaskoff, M., Chevrier, C. and Garlantézec, R., *Environ Res*, Aug 5 2025, Vol. 285, no. Pt 3, p. 122445.

Few studies have evaluated the impact of prenatal exposure to persistent organic pollutants (POPs) on menstruation characteristics. Therefore, the aim of our study was to investigate the associations between cord blood concentrations of POPs and menstruation characteristics including menarche status, menstrual regularity, pain and duration in girls at age 12. We used data from the French PELAGIE mother-child cohort follow-up at 12 years old which included a questionnaire on menstruation characteristics. POP concentrations of 14 organochlorine pesticides (OCPs), 17 polychlorinated biphenyls (PCBs), 5 polybrominated diphenyl ethers (PBDEs), and 9 per-polyfluoroalkyl substances (PFAS) were measured on cord blood sampled at birth. We used multivariate logistic regression and Poisson regression to study the relation between prenatal POPs and menarche status, regularity of menstruations, menstruation duration, and severe pain in the lower abdomen or cramps (N = 296). The effect of mixtures of POPs on these outcomes were assessed using quantile g-computation. The majority of POPs were associated with a non-statistically significant increased risk of menarche at 12 years old, especially for the PCB mixture (OR = 1.29, 95 % CI [0.99; 1.68]). We also observed a statistically significant association between the second tercile of dieldrin (OR = 2.91, 95 % CI [1.13; 7.82]) and PFNA (OR = 3.13, 95 % CI [1.01; 10.43]) and severe pain in the lower abdomen or cramps, and a statistically significant association between the second tercile of hexachlorobenzene and menstruation duration (% change = 25.6 %, 95 % CI [1.2; 56.6]). For others POPs and other menstrual characteristics we did not observe any associations. Further longitudinal studies are needed to confirm these results, possibly through combined analyses of several mother-child cohorts to increase study power.
https://doi.org/10.1016/j.envres.2025.122445

Bisphenol A exposure and behavioral outcomes in children: A systematic review and meta-analysis of evidence limited to the BASC assessment tool,
González-Palacios, P., Ramírez, V., Monteagudo, C., Zafra-Gómez, A. and Rivas, A., *Neuroscience and Biobehavioral Reviews*, Sep 2025, Vol. 176.

Background: The growing concern about exposure to endocrine disrupting chemicals (EDCs), and their effects on human health, especially the possible neurobehavioral effects in children, makes a review of the scientific evidence on the subject important. The study conducts a systematic review and applies meta-analysis to determine whether there is a relationship between bisphenol exposure and behavioral development in children, as measured by the Behavioral Assessment System for Children (BASC). Methods: In June and July 2024, Scopus, Web of Science, and Medline with PubMed were the databases used to search for studies within the scope of this study. A total of 562 articles were found, of which 59 were analyzed; finally, 13 studies met the inclusion criteria for systematic review and 7 for the meta-analysis. The scales measured in the different studies have been aggression, attention, hyperactivity, depression, anxiety and somatization; behavioral indices (behavioral symptom index, externalizing and internalizing behaviors) were also analyzed. Results: Most of the studies found no significant associations and no consistency in the results obtained. The heterogeneity in the design of the studies made it impossible to generate conclusive results in the application of meta-analysis. Discussion: There is a sex-based differentiation in the behavioral effects associated with bisphenol exposure, as bisphenols affect boys and girls differently, potentially through mechanisms involving estrogen receptors, among other biological pathways. Conclusions: Our study highlights the need to improve and homogenize the design and results of epidemiological studies to extract data effectively. More results are needed to be able to draw conclusions. https://doi.org/10.1016/j.neubiorev.2025.106274

Maternal exposure to pesticides and gestational diabetes mellitus in the Elfe cohort,
Guesdon, L., Warembourg, C., Chevrier, C., De Lauzon-Guillain, B., Caudeville, J., Charles, M. A., Le Lous, M., Blanc-Petitjean, P. and Béranger, R., *Environmental Research*, Nov 1 2025, Vol. 284.

Background: Gestational diabetes mellitus (GDM) increases risks of adverse perinatal outcomes and metabolic disorders in offspring. Some endocrine-disrupting chemicals are presumed to interfere with glucose metabolism. We aimed to assess the association between non-occupational exposures to pesticides and the risk of GDM. Methods: The study was conducted on 11 512 women (791 with GDM) from the French nationwide Elfe cohort. Among 114 suspected pesticides identified using a toxicogenomic approach, 62 with detection frequency >= 10 % were analyzed across three sources of exposure: residential use (self-reported, n = 18), agricultural (geographic information system, n = 14) and dietary (estimated by a food-frequency questionnaire and monitoring data of pesticide residues in foods, n = 30). The association between exposure to pesticides (no or low vs. high) and the occurrence of GDM was tested with single and multi-source adjusted logistic regression models. Results: In the multi-source model, dietary exposure to glyphosate (aOR = 0.6, 95 %CI: 0.5,0.9) or agricultural exposure (aOR = 0.8, 95 %CI:0.6,1.0) were associated with lower odds of GDM. The same effect was identified for two dietary pesticides: epoxiconazole (aOR = 0.6, 95 %CI: 0.5,0.8) and penconazole (aOR = 0.8, 95 %CI: 0.6,1.0). Dietary exposure to cypermethrin (aOR = 1.2, 95 %CI:1.0,1.5) and agricultural exposure to myclobutanil (aOR = 1.4, 95 %CI:1.1,1.9) were associated with higher odds of GDM. No significant association was identified for the residential use of pesticides. Conclusion: This toxico-genomic-based study identifies five pesticides associated with GDM through agricultural or dietary exposure. These findings provide new insights into environmental contributors to GDM. Further research is needed to elucidate the underlying toxicological mechanisms and confirm these associations.
https://doi.org/10.1016/j.envres.2025.122275

Sex-specific associations of the endocrine-disrupting chemicals with serum neurofilament light chain among US adults,
Hong, K. T., Cheng, H. Y., Zhuang, Y. and Yu, Y. X., *Ecotoxicology and Environmental Safety*, Jun 15 2025, Vol. 298.

Objective: Endocrine-disrupting chemicals (EDCs) can interfere with endocrine function and lead to neurological damage. Neurofilament light chain (NfL) is a protein released into the blood after neuroaxonal damage, and it has become a dependable biomarker for neurological conditions. The study aimed to investigate the associations between single or combined EDCs exposure and serum NfL levels in adults. Methods: The 1372 participants included in the study were from the 2013-2014 National Health and Nutrition Examination Survey. Due to the difference in types of EDCs, participants were divided into two populations. Multiple linear regression models were used to assess the association between 32 EDCs and NfL. The least absolute shrinkage and selection operator regression model was used for EDCs selection and the weighted quantile sum (WQS) regression was used for examining the association of EDCs mixture with NfL and identify the predominant exposure. Results: Levels of urinary bisphenol S, mono(2-ethylhexyl) phthalate, dibutyl phosphate, glyphosate, and 3,5,6-trichloropyridinol were positively associated with serum NfL levels, while benzophenone-3, methylparaben, and propylparaben showed negative associations. In the WQS regression model, the changes of NfL were 0.154 (95 % CI: 0.014-0.294) and 0.164 (95 % CI: 0.033-0.296) for each quartile increase in WQS index of EDCs mixture in the two populations, respectively. Analysis of the subgroup with gender stratification suggested that the association between EDCs mixture and NfL was only significant in men. The positive mixture beta was 0.219 (95 % CI: 0.056-0.380) and 0.257 (95 % CI: 0.082-0.433) in the two population, respectively. Conclusion: The study suggested a potential association between single or combined exposure to EDCs and NfL levels. High-level EDCs exposure might be associated with more severe neurological damage, particularly in men. https://doi.org/10.1016/j.ecoenv.2025.118272

Endocrine and Reproductive Health Considerations of Sunscreen UV Filters: Insights from a Comprehensive Review 2014-2024,
Jaskulak, M., Cinkusz, M., Franchuk, K. and Zorena, K., *Curr Environ Health Rep*, Aug 2 2025, Vol. 12, no. 1, p. 28.

PURPOSE OF REVIEW: Chemical (organic) ultraviolet (UV) filters-carbon-based compounds widely used in sunscreen formulations-are essential for protecting against harmful UV radiation. However, emerging evidence over the last decade (2014-2024) has raised concerns regarding their potential endocrine-disrupting effects, environmental persistence, and bioaccumulation. This comprehensive review evaluates the endocrine, reproductive, and developmental health impacts of organic UV filters, with a focus on benzophenone derivatives such as BP-3, BP-2, and 4-OHBP. RECENT FINDINGS: The analysis incorporates data from 75 studies identified through PRISMA-guided screening of epidemiological and human research. Findings reveal significant hormonal disruptions, including reduced testosterone levels in adolescent males, altered thyroid hormones in pregnant women, and associations with delayed pubertal development in boys and early menarche in girls. Mixed exposures to multiple UV filters, frequently occurring in real-world scenarios, demonstrate cumulative and complex effects, particularly on thyroid hormone levels and reproductive health. In men, benzophenones are associated with decreased sperm quality and motility, while in women, their impact on ovarian reserve and fertility outcomes appears less pronounced. Prenatal exposure studies show mixed outcomes, ranging from reduced neonatal size and gestational age to increased placental-to-birth weight ratios. This review underscores the dual nature of organic UV filters, emphasizing their importance in photoprotection while highlighting the need for a balanced

approach to safety evaluations. Future research should prioritize long-term cohort studies, assessments of mixed exposure effects, and the development of safer alternatives. Addressing these challenges is crucial for mitigating risks to human health and the environment while maintaining the protective benefits of sunscreens. https://doi.org/10.1007/s40572-025-00492-9

Understanding the role of endocrine disrupting chemicals as environmental obesogens in the obesity epidemic: A comprehensive overview of epidemiological studies between 2014 and 2024, Jaskulak, M., Zimowska, M., Rolbiecka, M. and Zorena, K., *Ecotoxicology and Environmental Safety*, Jul 1 2025, Vol. 299.

The prevalence of obesity has reached epidemic proportions worldwide, posing a significant public health concern due to its association with various chronic diseases and healthcare costs. In addition to traditional risk factors such as diet and physical activity, emerging evidence suggests that environmental pollutants, termed obesogens, may contribute to the obesity epidemic. Obesogens are endocrine-disrupting chemicals (EDCs) that can alter lipid homeostasis, promote adipogenesis, and disrupt metabolic regulation, leading to increased adiposity and obesity risk. This review explores available data from human studies published in the last decade, along with the mechanisms underlying obesogenic action, including their effects on adipocyte differentiation, adipose tissue development, and metabolic regulation. Overall, 75 studies were analyzed. Early-life exposure during critical developmental windows has been shown to increase obesity risk later in life, potentially through epigenetic modifications and transgenerational effects. Epidemiological studies provide evidence of associations between prenatal or early-life exposure and increased obesity risk in offspring. Additionally, study found more consistent associations between exposure to some EDCs (including phthalates, parabens, and bisphenols) and obesity or metabolic outcomes in children and women, while results for other chemicals (i.e. PFAS and organochlorine pesticides) were more heterogeneous, especially in adolescents and adults. Key findings indicate consistent associations between phthalate exposure and obesity in children, with mixed results for adults. Future research should focus on elucidating the full spectrum of obesogens, their mechanisms of action, and their implications for obesity risk across generations. This knowledge will inform preventive strategies and public health interventions aimed at addressing the obesity epidemic and its associated health burden. https://doi.org/10.1016/j.ecoenv.2025.118401

Associations of urinary organophosphate ester metabolites with bone mineral density in US children and adolescents aged 8-19 years: a cross-sectional study based on NHANES 2011-2018, Jin, H. L., Zhou, X. Y., Wang, X. Y. and Zhang, Y., *European Journal of Pediatrics*, Jun 4 2025, Vol. 184, no. 7.

Organophosphate esters (OPEs), widely used as alternative flame retardants and plasticizers, have been recognized for their bone toxicity. However, evidence linking OPE exposure to bone health in children and adolescents remains limited. We analyzed data from the 2011-2018 National Health and Nutrition Examination Survey, including 1576 participants aged 8-19 years. Five urinary OPE metabolites were measured-dibutyl phosphate (DBUP), bis(1-chloro-2-propyl) phosphate (BCPP), bis(2-chloroethyl) phosphate (BCEP), bis(1,3-dichloro-2-propyl) phosphate (BDCPP), and diphenyl phosphate (DPHP)-to examine their associations with BMD at the total body, lumbar spine, trunk, and pelvis. Weighted multivariable linear regression and restricted cubic spline models examined individual associations, while Bayesian kernel machine regression (BKMR) assessed mixture effects. Subgroup analyses were conducted by gender. DBUP was negatively correlated with BMD at multiple sites, total body BMD beta = - 0.016 (95% CI: - 0.030, - 0.002), trunk BMD beta = - 0.019 (95% CI: - 0.032, - 0.005), and pelvis BMD beta = - 0.028 (95% CI: - 0.048, - 0.007). BCPP, BCEP, BDCPP, and DPHP exhibited site-specific associations. DPHP showed a nonlinear dose-response with

total-body and trunk BMD. BKMR confirmed a negative mixture effect, with DBUP contributing most. Subgroup analyses suggested that its effect on BMD was more significant in males.Conclusions: Individual and combined OPE exposure in children and adolescents was inversely associated with bone mineral density, with gender differences. However, due to the cross-sectional research design, these findings should be interpreted with caution and need to be verified in future longitudinal studies. What is Known:center dot OPEs, widely used as flame retardants and plasticizers, have been recognized both as potential endocrine disruptors and for their bone toxicity.center dot Prior studies on the association between OPE exposure and BMD have mainly focused on adult populations, with limited evidence in children and adolescents.What is New:center dot This study is the first to investigate the association between urinary OPE metabolites and BMD across multiple skeletal sites among U.S. children and adolescents aged 8-19 years using NHANES data.center dot Individual and combined OPE exposures were inversely associated with BMD, with site- and gender-specific variations; DBUP showed the strongest effect. These findings suggest that early-life OPE exposure may impair bone health, highlighting the need for longitudinal studies. https://doi.org/10.1007/s00431-025-06235-0

Paraben exposure profiles in pregnant women and association with changes in thyroid hormone levels,
Khelfi, A., Idjeraoui, A., Ouarzidini, H., Aksas, K., Makrelouf, M., Cherifi, M. and Azzouz, M., Ann Endocrinol (Paris) . 2025 Jun 13;86(5):101801

Parabens are widely suspected to be endocrine disruptors. Exposure during pregnancy may interfere with thyroid hormone homeostasis, resulting in adverse effects on neurodevelopment and fetal growth.This study aimed to assess pregnant women's exposure to parabens and possible associations with changes in thyroid hormone levels during pregnancy. Links between exposure sources and endogenous paraben concentrations was also investigated.A descriptive study included 384 pregnant women. Thyroid hormones and thyroid-stimulating hormone (TSH) were measured on electrochemiluminescence. Parabens (methylparaben (MP), ethylparaben (EP), and propylparaben (PP)) were detected on LC-MS/MS.Parabens were found in almost all pregnant women (MP: 96.9%; EP: 89.3%; PP: 94.5%), at varying ranges of µg/g creatinine (MP: 36.633 ± 39.849; EP: 9.721 ± 15.655; PP: 22.109 ± 20.722). There were significant negative associations between urinary concentrations of PP and plasma levels of TSH and free thyroxine (FT4). Analysis of exposure sources revealed significant associations of urinary levels of EP with exposure to facial care products and sunscreens.This research highlights the alarming rate of exposure to parabens, which may have deleterious effects on thyroid hormone levels in pregnant women, with consequent repercussions on fetal neural development. https://doi.org/10.1016/j.ando.2025.101801

Exposome-wide association study of sex-steroid hormones in the US general population: evaluation of complex mixture effects☆,
Lee, J., Jang, H. and Shin, H. M., *Environmental Pollution*, Sep 1 2025, Vol. 380.

Previous research on environmental chemicals and sex-steroid hormones predominantly focused on specific chemical classes, with limited assessments of mixture effects. This study addressed this gap through an exposome-wide association study (ExWAS). We analyzed data from the National Health and Nutrition Examination Survey (NHANES, 2013-2014 and 2015-2016), incorporating measurements of sex-steroid hormones (total testosterone [tT], estradiol [E2], and sex hormone-binding globulin [SHBG]) and environmental chemical biomarkers from 9,172 participants. Analyses were stratified into six sex- and age-specific subgroups to account for distinct variations in hormone profiles among participants. Robust regression, which accounts for outliers, was employed to identify biomarkers associated with hormone levels. Quantile g-computation was applied to assess

mixture effects using the identified biomarkers with a detection rate of >= 70%. Furthermore, we visualized exposure-hormone interaction networks. Survey weights were accounted for in all analyses. After adjustment for multiple comparisons, we identified 2 to 32 biomarkers significantly associated with at least one hormone within each of the six subgroups. Males exhibited approximately twice the number of significant biomarker associations compared to females. Concurrent exposure to multiple chemical biomarkers was associated with hormone levels, with pronounced associations observed in adolescent boys ((3 = -0.364, 95% CI: -0.497, -0.230 for tT, and (3 = -0.350, 95% CI: -0.583, -0.117 for E2). Network analysis revealed direct associations between specific biomarkers (e.g., lead and copper) and hormones. Our findings suggest that environmental chemicals, both individually and in mixtures, are associated with alterations in sex-steroid hormones, with adolescents showing potential vulnerability to exposure-related endocrine disruption. https://doi.org/10.1016/j.envpol.2025.126533

Prenatal exposure to polyfluoroalkyl substances and visual acuity in preschool children: Findings from the Guangxi Zhuang birth cohort in China,
Lei, L. D., Lv, F. F., Lu, P. N., Mo, C. M., Li, J. X., Xu, X. M., Wei, G. J., Huang, X. Q., Qiu, X. Q., Huang, D. P., Zhou, X. M., Wei, H., Zeng, X. Y. and Liu, S., *Ecotoxicology and Environmental Safety*, Jul 15 2025, Vol. 300.

Background: Prenatal exposure to Polyfluoroalkyl Substances (PFASs) had been associated with adverse effects on multiple systems in offspring. However, the effects on visual system had not been previously explored. Objective: The study aimed to assess the association between prenatal exposure to PFASs and visual acuity and visual impairment in preschool children. Methods: A total of 1008 mother-infant pairs were extracted from the Guangxi Zhuang Birth Cohort in China. Maternal serum concentrations of nine PFASs were measured using Ultra-Performance Liquid ChromatographyMass Spectrometry (UPLC-MS). The preschool visual acuity (VA) in the offspring was obtained through the local maternal and child health information system. Multiple linear regression models and logistic regression models were performed to study the single effects of individual PFAS on VA and visual impairment (VI), respectively. Additionally, Bayesian kernel machine regression (BKMR) and quantile g-computation (Qgcomp) models were utilized to assess the joint effects of the nine PFASs. Results: Prenatal exposure to PFOS ((3 = 0.074, 95 % CI: 0.033, 0.116), PFHxS ((3 = 0.062, 95 % CI: 0.012, 0.111), and PFBS ((3 = 0.023, 95 % CI: 0.001, 0.044) exhibited significant positive associations with enhanced VA. Conversely, PFOS (OR = 0.481, 95 % CI: 0.245, 0.946) and PFHxS (OR = 0.450, 95 % CI: 0.244, 0.830) were significantly associated with reduced odds of VI. BKMR and quantile g-computation (Qgcomp) modeling consistently displayed positive joint-effects for nine PFASs mixtures on VA. Stratified analysis by sex indicated that certain significant associations were observed exclusively in boys or girls, and these associations were positively correlated with VA. Conclusions: The evidence does not substantiate the hypothesis that prenatal exposure to PFASs adversely impacts visual development. Nonetheless, inverse associations reported here should not be interpreted as protective, as these associations might be driven by some unresolved confounding factors and biases. Their relationship still needs to be elucidated in future studies, using larger samples and accounting for both prenatal and childhood periods. https://doi.org/10.1016/j.ecoenv.2025.118477

Association of urine parabens with liver function in US adolescents based on NHANES 2007-2016,
Li, L. F., Hu, G. C., Luo, X., Wei, Z. X. and He, J., *Scientific Reports*, Jul 1 2025, Vol. 15, no. 1.

Paraben esters are commonly used as preservatives in cosmetics, personal hygiene products, food and drugs. However, there is a lack of evidence regarding the impact of exposure to Paraben esters on adolescent liver function. We analyzed data from the 2007-2016 National Health and Nutrition

Examination Survey (NHANES). Finally, a random sample of 1845 adolescents aged 12 to 19 was selected for the study. The effect of urinary parabens on liver function indexes was analyzed using weighted linear regression to ensure accurate representation of the population. Then, we applied the weighted quantile sum (WQS) analysis and the Bayesian kernel machine regression (BKMR) to examine the associations between parabens and liver function indicators. Based on the results from three different models, four parabens and their total were negatively associated with Albumin (ALB) and Alkaline Phosphatase (ALP), and positively associated with Total Bilirubin (TBIL). Moreover, among the parabens, butyl paraben and propyl paraben had the highest weights. Overall, our results indicate that parabens are significantly but weakly associated with changes in liver function in US adolescents. Further research is needed to explore these relationships.
https://doi.org/10.1038/s41598-025-08435-y

The association between brominated flame retardants and serum testosterone levels in American adult men: NHANES 2013-2016,
Li, X., Chen, M., Zheng, Q., Wang, Z., Lin, D. and Peng, M., *Front Public Health*, 2025, Vol. 13, p. 1589047.

BACKGROUND: Brominated flame retardants (BFRs), especially polybrominated diphenyl ethers (PBDEs), are commonly utilized, yet their possible endocrine-disrupting effects have sparked significant concerns. Nonetheless, the link between exposure to BFRs and serum testosterone levels in adult males is still not well comprehended. METHODS: We analyzed data from 1,150 men aged ≥20 years from the National Health and Nutrition Examination Survey (NHANES) in 2013-2016. Serum concentrations of BFRs (PBDE congeners: PBDE-28, PBDE-47, etc.) and testosterone levels were measured via mass spectrometry and liquid chromatography-tandem mass spectrometry, respectively. Free testosterone (FT) and bioavailable testosterone (BAT) were calculated using the Vermeulen equation, based on measured total testosterone (TT), sex hormone-binding globulin (SHBG), and serum albumin concentrations. Linear regression models were used to evaluate the association between BFRs and TT, BAT, FT, and SHBG, adjusting for confounders including age, race, and lifestyle factors. We also evaluated potential associations modified by age, and conducted a sensitivity analysis to assess the robustness of the observed associations. RESULTS: After all continuous variables were log2-transformed and potential confounders were adjusted, significant inverse associations were found between PBDE-28 and PBDE-47 levels with TT (β = -0.641, 95% CI: -1.098, -0.185) and FT (β = -0.883, 95% CI: -1.616, -0.149). Specifically, in the stratified analysis, older men (≥60 years) showed stronger associations between PBDE-28 and PBDE-47 exposure with lower testosterone levels (β = -0.892, 95% CI: -1.472, -0.311 for PBDE-28 and β = -0.695, 95% CI: -1.199, -0.191 for PBDE-47). Sensitivity analysis confirmed that PBDE-28 and PBDE-47 were consistently associated with reduced testosterone and free testosterone levels, with the associations remaining significant even after adjusting for potential co-exposures and lifestyle factors. CONCLUSION: Our findings suggest that exposure to PBDE-28 and PBDE-47 is associated with lower testosterone levels, particularly in older men. These results highlight the potential reproductive risks posed by BFR exposure, warranting further investigation into the long-term health impacts.
https://doi.org/10.3389/fpubh.2025.1589047

Association between ovarian reserve and organophosphate flame retardants in women of childbearing age,
Lien, H. T., Ou, Y. C., Cheng, Y. H., Kung, C. T., Chang, Y. C., Weng, P. L. and Lan, K. C., *Taiwanese Journal of Obstetrics & Gynecology*, May 2025, Vol. 64, no. 3, p. 504-511.

Objective: This study aimed to investigate the association between organophosphate flame retardants (OPFRs) and ovarian reserve in women of childbearing age. Materials and methods: In

this Cross-sectional study, the participants were recruited from August 2020 to October 2022 at the outpatient department of Obstetrics and Gynecology in Chang Gung Memorial Hospital, Kaohsiung Medical Center in Taiwan. The inclusion criteria were as follows: adult women of childbearing age were eligible to participate. Old age (>50 years old), patients using antidepressants and antipsychotics for over months were excluded. We measured the urinary concentrations of 10 OPFR compounds to assess exposure patterns and compared the clinical and urinary OPFR profiles among subgroups to determine whether these OPFR compounds were independently correlated with AMH, FSH, and LH levels. Environmental and lifestyle factors were assessed using questionnaires to determine the risk factors for OPFR exposure. Results: Total 99 participants were enrolled in our study. after adjusting for covariates, higher urinary concentrations of bis(1,3-dichloro-2-propyl) phosphate (BDCPP) and diphenyl phosphate (DPHP) were predictors of the lower AMH subgroup compared to the high AMH subgroup (low vs. high AMH (cut-off value: 1.5 ng/mL), odds ratio (OR) (95 % confidence interval (CI)), 5.714 (1.435-22.727), p = 0.007; 4.149 (1.004-17.241), p = 0.037, respectively). FSH and LH levels were not significantly associated with the 10 OPFRs in our study. Conclusion: Our study revealed that OPFR exposure was widespread among women of childbearing age, with a 100 % detection rate in urinary samples. Additionally, higher urinary concentrations of BDCPP and DPHP were predictors of the lower AMH subgroup compared to the high AMH subgroup. Further research is required to gain a deeper understanding of the exposure patterns and potential reproductive toxicity of OPFRs in women of childbearing age. (c) 2025 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
https://doi.org/10.1016/j.tjog.2024.11.012

Associations between organophosphate flame retardants and risk for nonsyndromic cleft lip and/or palate in offspring,
Lin, S. J., Li, S. N., Cheng, Q. H., Ding, Y. Q., Chen, Y. Y., Liu, J. F., Jin, L., Li, Z. W., Ren, A. G. and Wang, L. L., *Environmental Sciences Europe*, Jun 22 2025, Vol. 37, no. 1.

IntroductionNonsyndromic cleft lip and/or palate (NSCL/P) is a common congenital malformation with a complex etiology involving many environmental factors. Organophosphate flame retardants (OPFRs) are a class of emerging contaminants that are associated with adverse reproductive and developmental outcomes, but their potential role in NSCL/P risk remains unexplored.MethodsA total of 134 NSCL/P cases and 292 controls were recruited in China between 2005 and 2021. The concentrations of six target OPFRs in placentas were quantified using gas chromatography-tandem mass spectrometry. Logistic regression, Bayesian kernel machine regression (BKMR), and weighted quantile sum (WQS) regression were employed to examine the relationships between OPFR exposure and NSCL/P risk.ResultsIn the logistic regression model, high TBP level was associated with an increased risk for NSCL/P, while low TCPP level was linked to elevated risk for NSCL/P. The BKMR model revealed a significant joint effect of mixed exposure to OPFRs on the increased risk for NSCL/P, with TBP associated with a significant increase in NSCL/P risk. In the WQS model, the WQS index was positively correlated with the risk for NSCL/P [odds ratio (OR) = 1.15, 95% confidence interval (CI): 1.07, 1.24], with TBP having the highest weight of 90%.ConclusionsThis study provides novel epidemiologic evidence that prenatal exposure to a mixture of OPFRs may lead to an increased risk of NSCL/P, to which TBP is a major contributor. These findings underscore the importance of reducing environmental OPFR exposures during fetal development to mitigate the burden of this common birth defect. https://doi.org/10.1186/s12302-025-01150-5

Evaluating the relationship between environmental chemicals and obesity: Evidence from a machine learning perspective,

Liu, H., Gu, H. W., Li, J., Fang, Y. F., Yang, S. and Liang, G. Y., *Ecotoxicology and Environmental Safety*, Jul 15 2025, Vol. 300.

Environmental chemicals are increasingly recognized as important contributors to obesity, yet the number of studies evaluating this relationship remains insufficient. This study aimed to investigate these associations using interpretable machine learning techniques. Data from 1183 participants in the 2011-2012 National Health and Nutrition Examination Survey were analyzed. Several machine learning models, including Support Vector Machines, Random Forest, k-Nearest Neighbors, Naive Bayes, AdaBoost, and XGBoost, were employed to predict generalized and abdominal obesity using environmental chemical exposures and demographic information. The XGBoost model was further explored for its ability to interpret variable contributions, utilizing SHapley Additive exPlanations (SHAP) to identify key predictors. Logistic regression models revealed that 4-OH-PHEN, 2-OH-NAP, and 2-OH-PHEN were positively associated with generalized obesity, whereas UMo and 3-OH-FLUO exhibited negative associations. Similarly, 4-OH-PHEN demonstrated a positive association with abdominal obesity, whereas 3-OH-FLUO, USr, and BPb were negatively associated. To further examine these relationships, dose-response associations between environmental chemicals and obesity were analyzed using restricted cubic spline plots. A nonlinear relationship was identified between UMo and obesity (P-nonlinear=0.016). Mediation analysis revealed that blood lipids partially mediated the relationship between certain environmental chemicals and obesity. This study underscores the importance of interpretable machine learning in understanding the complex associations between environmental chemicals and obesity. It identified specific chemicals associated with generalized and abdominal obesity and shed light on the mediating role of blood lipids. These findings contribute to the growing body of evidence on the role of environmental exposures in obesity and provide potential pathways for future research and interventions.
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The significance of organophosphate flame retardants in patients with esophageal squamous cell carcinoma,
Lu, H. I., Huang, W. T., Lee, W. C., Cheng, F. J., Kung, C. T., Wang, C. C., Wang, L. J., Ou, Y. C. and Li, S. H., *Environmental Geochemistry and Health*, Jul 2025, Vol. 47, no. 7.

Esophageal squamous cell carcinoma (ESCC) is a leading cause of cancer-related mortality in Taiwan, and has a poor prognosis despite treatment advances. Emerging evidence suggests environmental contaminants, including organophosphate flame retardants (OPFRs), as potential cancer contributors. This study aims to investigate the association between exposure to OPFRs and ESCC. A case-control study with 133 ESCC patients and 133 controls was conducted. Urinary concentrations of 10 OPFRs, including 5 triesters (TDCPP, TCEP, TBEP, TNBP, TPHP) and their corresponding diesters (BDCPP, BCEP, DBEP, DNBP, DPHP), were measured using UPLC-MS/MS, and the associations between OPFR levels and ESCC risk was analyzed. Survival analyses were also performed to assess prognostic impact. In vitro and in vivo experiments were conducted to explore cytotoxic effects and pathological changes induced by OPFRs, with pathways identified via RNA sequencing and gene set enrichment analysis (GSEA). Higher detection rates of BDCPP, BCEP, and TDCPP were observed in ESCC patients, with TDCPP showing the strongest association with ESCC (odds ratio [OR] = 2.58, p = 0.005) and the poorest survival outcome (hazard ratio [HR] = 1.91, p = 0.021). In cell culture experiments, TDCPP induced cytotoxicity, oxidative stress, and inhibited colony formation. In a murine animal model, combined TDCPP and 4-NQO exposure led to a significantly higher incidence of ESCC compared to 4-NQO alone. RNA sequencing and GSEA analysis identified several differentially expressed genes and pathways related to immune response and cellular stress. This study highlights TDCPP as a potential environmental risk factor for ESCC, emphasizing the

importance of considering environmental exposures in patients with ESCC, and the need for further research into the carcinogenic impact of OPFRs. https://doi.org/10.1007/s10653-025-02599-2

Per-and Polyfluoroalkyl Substances in Eutopic Endometrium Tissue and Risk of Endometriosis: Findings from the Investigating Mixtures of Pollutants and Endometriosis in Tissue (IMPLANT) Study,
Marroquin, J. M., Krall, J. R., Schliep, K. C., Farland, L. V., Krishnamoorthi, V., Kannan, K. and Pollack, A. Z., *Environmental Health Perspectives*, Jun 2025, Vol. 133, no. 6.

Background: Per- and polyfluoroalkyl substances (PFAS) exposure is widespread and has been linked with gynecologic disease. To our knowledge, no study has measured PFAS in endometrial tissue. Methods: Eutopic endometrial tissue specimens (n=434) were collected from Investigating Mixtures of Pollutants and Endometriosis in Tissue (IMPLANT) study participants undergoing laparoscopy or laparotomy for any indication (2007-2009). Nine PFAS were measured by high-performance liquid chromatography-tandem mass spectrometry [perfluorodecanoic acid (PFDA), perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorododecanoic acid (PFDoDA), perfluoroheptanoic acid (PFHpA), perfluorooctanesulfonamide (PFOSA), and perfluoroundecanoic acid (PFUnDA)]. Surgeons diagnosed endometriosis by gold-standard visualization and evaluated the endometriosis staging as moderate and severe (stages 3 and 4) compared to minimal and mild (stages 1 and 2) using American Society of Reproductive Medicine (ASRM) classification. We used modified Poisson regression models adjusted for age (continuous), race (white, all other race/ethnicities), smoking status (serum cotinine >10 ng/mL), study site (Utah, California), and body mass index (continuous) to obtain relative risks (RR) of endometriosis diagnosis and 95% confidence intervals (CIs) for each PFAS. PFAS mixtures were evaluated using Bayesian kernel machine regression. Results: Participants were, on average, 33 +/- 7 years old, and 75% of participants were non-Hispanic white. Of the 181 participants with an incident endometriosis diagnosis, 73% had ASRM stage 1 or 2, while 27% had stage 3 or 4. Median [interquartile range (IQR)] eutopic endometrium tissue levels, in nanograms per gram, were 6.58 (6.44) for PFOS, 1.93 (1.71) for PFOA, 0.65 (0.75) for PFHxS, 0.58 (0.52) for PFNA, and 0.12 (0.18) for PFOSA. PFAS in the endometrial tissue was not associated with endometriosis. However, select PFAS in the eutopic tissue were associated with a risk of more advanced (stage 3 or 4 vs. 1 or 2) endometriosis [PFOSA RR=1.25 (95% CI: 1.10, 1.43), PFHxS RR=1.37 (95% CI: 1.12, 1.68), PFOS RR=1.36 (95% CI: 1.02, 1.81)]. Conclusion: PFAS were widely detected in eutopic endometrial tissue. There was no evidence that PFAS in endometrial tissue were associated with a higher risk of endometriosis diagnosis. However, PFOS, PFOSA, and PFHxS in the endometrial tissue were associated with risk of more severe stage of endometriosis.
https://doi.org/10.1289/ehp15852

Exposure to per- and poly-fluoroalkyl substances in association to later occurrence of type 2 diabetes and metabolic pathway dysregulation in a multiethnic US population,
Midya, V., Yao, M., Colicino, E., Barupal, D., Lin, X., Gennings, C., Chatzi, L., Setiawan, V. W., Loos, R. J. F., Walker, R. W., Walker, D. I. and Valvi, D., *EBioMedicine*, Aug 2025, Vol. 118, p. 105838.

BACKGROUND: Growing evidence suggests that exposure to per- and polyfluoroalkyl substances (PFAS) are linked to an increased risk of type 2 diabetes (T2D); however, the effect of PFAS mixtures and underlying mechanisms are not well understood. We examined the associations between exposure to PFAS mixture with later T2D diagnosis and underlying metabolic dysregulations. METHODS: We conducted a nested case-control study within BioMe, an electronic health record-linked biobank of >65,000 patients seeking primary care at Mount Sinai Hospital, New York, since 2007. After excluding prevalent T2D cases at baseline, we selected 180 incident T2D cases (33%

African Americans, 33% Hispanics, 33% Whites) and 180 age, sex, and ancestry-matched T2D-free controls. In prediagnostic plasma collected at baseline (~6 years before diagnosis), we quantified seven PFAS and untargeted metabolomic profiles. We used Weighted Quantile Sum regression to evaluate the PFAS mixture association with the odds for incident T2D. We analysed the associations between ~650 annotated metabolites and the PFAS mixture or T2D odds using Hierarchical Bayesian Weighted Quantile Sum and logistic regression, respectively, adjusting for matching factors and other confounders. Pathway enrichment analyses were performed using Mummichog. FINDINGS: Each tertile increase in the PFAS mixture was associated with higher odds of incident T2D (OR [95% CI] = 1.31 [1.01, 1.70]), with Perfluorooctane Sulfonate (PFOS) having the highest contribution to this association. Metabolites associated with both the PFAS mixture and T2D odds were 5-hydroxytryptophan, glucoheptulose, and sulfolithocholylglycine; the associations with sulfolithocholylglycine survived multiple testing corrections. Pathways associated with both the PFAS mixture and T2D were glutamate metabolism, arginine and proline metabolism, and drug metabolism-cytochrome p450. INTERPRETATION: Exposure to PFAS mixtures may be associated with increased odds for T2D in multiethnic populations via dysregulations in amino acid and drug metabolism. Larger investigations in multiethnic populations are required to elucidate the potential PFAS contribution to metabolic alterations and T2D risk. FUNDING: National Institutes of Health (R01ES033688, P30ES023515, R21ES035148, R35ES030435, R01ES032242, R01ES034521, R01ES029944, R01ES030364, U01HG013288, R21ES037112 and P30ES007048).
https://doi.org/10.1016/j.ebiom.2025.105838

Associations between urinary phthalate metabolite mixtures, semen quality, and serum reproductive hormone levels in Japanese men seeking fertility treatment,
Mizuno, Y., Yamasaki, K., Uchida, M., Iwamoto, T. and Konishi, S., *Reproductive Toxicology*, Sep 2025, Vol. 136, p. 8.

Phthalate mixtures may adversely affect men's reproductive functioning. This study aimed to analyze the association between exposure to phthalate mixtures, semen quality, and reproductive hormone concentrations in Japanese men seeking fertility treatment. This cross-sectional study analyzed data from 197 Japanese adult males who visited clinics for infertility consultations in 2020 and 2021. Semen samples were collected to measure volume, sperm count, sperm concentration, and motility. Spot urine samples were collected to quantify phthalate monoesters, specifically phthalate diester metabolites, using liquid chromatography-tandem mass spectrometry. Serum concentrations of testosterone, estradiol, luteinizing hormone, follicle-stimulating hormone, and prolactin were obtained from clinical records. Three statistical methods-weighted quantile sum regression, quantile g-computation, and Bayesian kernel machine regression-were applied. Urinary concentrations of phthalate metabolite mixtures were positively associated with sperm motility, with monoethyl phthalate being the most important contributor to the observed association. No significant associations were found between phthalate mixtures and semen volume, sperm count, or concentration. These associations were consistent across all three statistical methods. Higher urinary concentrations of phthalate metabolite mixtures were associated with lower testosterone and higher prolactin concentrations in serum; however, there were no significant associations between phthalate mixtures or individual phthalate metabolites and estradiol, folliclestimulating hormone, or luteinizing hormone concentrations. Higher exposure to phthalate mixtures may be associated with increased sperm motility and serum prolactin and reduced serum testosterone concentrations. Overall, these findings suggest that even at a relatively low level, exposure to phthalate mixtures may affect male reproductive health.
https://doi.org/10.1016/j.reprotox.2025.108957

Per- and polyfluoroalkyl substance concentrations during pregnancy and at birth and risk of childhood acute lymphoblastic leukemia,
Morimoto, L. M., Metayer, C., Dolios, G., Wiemels, J. L., Ma, X., Guan, H., Maroli, A. and Petrick, L. M., *Environ Res*, Jul 25 2025, Vol. 285, no. Pt 3, p. 122436.

BACKGROUND: Per- and polyfluoroalkyl substances (PFAS) comprise a class of persistent environmental pollutants with potential carcinogenic effects, but their impact on childhood cancer remains underexplored. A child's exposure to PFAS can occur through various pathways postnatally, including contaminated food, water, and consumer products; and in utero, as PFAS can cross the placenta. METHODS: To investigate the association between early-life PFAS exposure and the risk of childhood acute lymphoblastic leukemia (ALL), we analyzed archived blood samples from children diagnosed with ALL and matched cancer-free controls. Using novel untargeted liquid chromatography-high resolution mass spectrometry (LC-HRMS), we measured PFAS levels in paired maternal pregnancy and child newborn blood samples. RESULTS: Our study identified an independent association between MeFOSAA levels at birth and increased ALL risk, particularly among children diagnosed at 2 years of age or younger. MeFOSAA measured in maternal second-trimester blood showed a weak association with ALL, although it was not statistically significant. CONCLUSIONS: These results suggest that early-life exposure to MeFOSAA may play a critical role in the development of childhood ALL. Our findings corroborate previous reports linking MeFOSAA exposure during pregnancy to childhood ALL, highlighting its potential carcinogenicity during key developmental windows. https://doi.org/10.1016/j.envres.2025.122436

Prenatal exposure to phthalates and alternative plasticizers and emotional and behavioral outcomes in early childhood in the Environmental influences on Child Health outcomes (ECHO) cohort,
Oh, J., Buckley, J. P., Upadhyaya, S., Kannan, K., Barrett, E. S., Bastain, T. M., Breton, C., Eick, S. M., Geiger, S. D., Ghassabian, A., Habre, R., Herbstman, J. B., Hirtz, D., Liang, D. H., Lewinn, K., Meeker, J. D., O'connor, T. G., Hertz-Picciotto, I., Ruden, D., Sathyanarayana, S., Schantz, S. L., Schweitzer, J. B., Sigal, A., Woodruff, T. J., Zhao, Q., Schmidt, R. J., Bennett, D. H. and Consortium, E. C., *Environment International*, Aug 2025, Vol. 202.

Background: Evidence suggests prenatal phthalate exposure adversely affects children's behavior. However, epidemiological studies on alternative plasticizers remain scarce. This study investigated associations of gestational exposure to phthalates and alternative plasticizers with internalizing and externalizing behaviors in children aged 1.5-5 years. Methods: The study included 2617 mother-child dyads from 13 Environmental influences on Child Health Outcomes (ECHO) cohorts. Maternal urine samples, primarily collected mid-to late-pregnancy, were analyzed for 27 phthalate metabolites and 6 alternative plasticizer metabolites. Based on detection frequency, metabolite concentrations were modeled either continuously or categorically (Group 1: non-detectable, 2: lower detectable, higher detectable). Covariate-adjusted associations between individual metabolite concentrations and internalizing and externalizing T-scores on the Child Behavior Checklist for Ages 11/2-5 were estimated using linear mixed-effects models. Effect modification by child sex was also examined. Results: An interquartile range increase in mono-benzyl phthalate (MBzP) and membership in Group 3, versus Group 1, for mono-hexyl phthalate (MHxP) were associated with higher externalizing T-scores (next for continuous MBzP = 0.53, 95% CI: 0.05, 1.00; next for MHxP Group 3 = 1.23, 95% CI: 0.35, 2.12). We observed no robust associations between phthalate metabolites and internalizing T-scores, nor between cyclohexane-1,2-dicarboxylic acid mono carboxyisooctyl ester (DINCH) metabolites and any behavioral outcomes. Child sex modified associations between several metabolites and externalizing T-scores, although the direction of effect varied by metabolite. Conclusion: This large-scale study suggests that prenatal exposure to several phthalates, but not to

the alternative plasticizer DINCH, may be associated with a small-to-modest increase in externalizing behaviors in young children. https://doi.org/10.1016/j.envint.2025.109647

Sex-specific effects of prenatal exposure to phthalates and bisphenol A on adverse birth outcomes: Results from The Korean CHildren's ENvironmental health Study (Ko-CHENS),
Oh, J., Shah, S., Lee, K. A., Park, E., Lee, D. W., Hong, Y. C., Song, S., Kim, S. Y., Park, H., Kim, H. C., Jeong, K. S., Ha, E. and Ko, C. S. G., *Environment International*, May 2025, Vol. 199.

Objectives: Although previous epidemiological studies have reported the effects of fetal exposure to phthalates and phenols on birth outcomes, evidence is still limited. The objective of this study was to investigate whether prenatal exposure to endocrine-disrupting chemicals [EDCs; phthalates and bisphenol A (BPA)] is associated with birth outcomes and whether there are sex-specific effects. Methods: We used data from the Korean CHildren's ENvironmental health Study (Ko-CHENS) cohort. Exposure to phthalates and BPA was measured by urine tests, and the information on outcomes and confounders was obtained from delivery records, biomarker assessment, and a self-reported questionnaire. We performed multivariate logistic regression to estimate the association between exposure to individual phthalates and bisphenol A and birth outcomes. Additionally, to evaluate the effects of EDC mixture exposure, we performed weighted quantile sum regression analysis. Subgroup analysis stratified by maternal age and sex at birth was performed to examine potential differences in associations. Results: This study included 2,176 mother-child pairs from the Ko-CHENS. We observed a significant association between the risk of PTB and exposure to BPA during early pregnancy and mono-carboxyoctyl phthalate (MCOP) during late pregnancy, with odds ratios of 1.23 (95% CI: 1.01, 1.49) and 1.29 (95% CI: 1.03, 1.62), respectively. Additionally, there was a significant association between exposure to MCOP during early pregnancy and the risk of LBW (OR: 1.39, 95% CI: 1.03, 1.89). For male infants in particular, exposure to MCOP during early pregnancy was associated with the risk of LBW (OR: 2.44, 95% CI: 1.43, 4.15), and exposure to MCOP during late pregnancy was associated with the risk of PTB (OR 1.45, 95% CI: 1.05, 2.02). Conclusions: This study suggests a potential association between exposure to BPA during early pregnancy and PTB, while exposure to MCOP during late pregnancy was associated with increased PTB risk in male infants. https://doi.org/10.1016/j.envint.2025.109518

Association of Per- and Polyfluoroalkyl Substances with Pan-Cancers Associated with Sex Hormones,
Olarewaju, E. and Obeng-Gyasi, E., *Toxics*, Jun 14 2025, Vol. 13, no. 6.

Per- and polyfluoroalkyl substances (PFASs) are ubiquitous environmental contaminants with potential endocrine-disrupting properties. This study examines the association between exposure to multiple PFASs and pan-cancers associated with sex hormones (PCSH) while accounting for potential non-linear relationships and interactions. We analyzed data from the National Health and Nutrition Examination Survey (NHANES), spanning two-year cycles from 1999 to 2012 and including 14,373 participants. Serum concentrations of six PFAS-perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorohexanesulfonic acid (PFHxS), perfluorodecanoic acid (PFDE), perfluorononanoic acid (PFNA), and perfluoroundecanoic acid (PFUA)-were assessed for their relationship with PCSH. The statistical analyses included descriptive statistics, Spearman and Pearson correlation analyses, and both linear and logistic regression models. Additionally, Bayesian kernel machine regression (BKMR) was applied to capture potential nonlinear relationships and interactions. The initial t-tests showed a statistically significant difference in PFOS levels between individuals with and without PCSH ($p = 0.0022$), with higher mean PFOS levels in the PCSH group. Chi-square tests revealed a significant association between ethnicity and PCSH ($p < 0.001$). Linear and logistic regression analyses revealed significant associations for PFOS. BKMR analysis identified

PFOA as having the highest posterior inclusion probability, indicating its importance in explaining PCSH risk. Univariate exposure-response analysis revealed limited individual PFAS effects. However, bivariate analysis indicated a complex U-shaped interaction pattern among many joint PFAS assessments. The overall exposure effect analysis suggested that the combined impact of all PFASs was more strongly associated with PCSH at exposure levels below the 0.5 quantile compared to higher levels. Single-variable interaction analyses highlighted PFOA and PFOS as the most interactive PFASs when evaluating their interaction with combined exposure to all other PFASs. In summary, while the initial findings suggested a positive association between PFOS and PCSH, the BKMR analysis revealed complex non-linear relationships and interactions among PFAS. These findings highlight the importance of evaluating PFASs as a mixture rather than as individual chemicals and using techniques that can capture non-linear relationships and interactions.
https://doi.org/10.3390/toxics13060501

The relationship between metabolic syndrome and environmental endocrine disruptors: A systematic review and meta-analysis,
Pan, K., Xu, J., Li, F., Aris, A. Z., Yu, H., Xu, Y., He, J., Wang, C. and Yu, J., *iScience*, Jul 18 2025, Vol. 28, no. 7, p. 112907.

Metabolic syndrome (MetS) is considered to be an important factor leading to an increased risk of chronic non-communicable diseases. Studies have found that exposure to environmental endocrine disruptors (EEDs) is associated with MetS, but the relationship between the two is unclear. In order to clarify the relationship between the two, a systematic review and meta-analysis were conducted to investigate their association. We searched Web of Science databases, Embase, and PubMed. We then utilized I(2) statistics to assess the literature heterogeneity and pooled the data using both fixed-effects model (I(2) < 50%) and the random effects model (I(2) > 50%) in accordance with the PRISMA guidelines. The results showed that exposure to perfluoroalkyl substances (PFASs) was associated to specific components of MetS, such as PFNA and "high waist circumference" (OR = 1.23, 95% CI: 1.10-1.38), and PFOA and "elevated blood pressure" (OR = 1.05, 95% CI: 1.01-1.08). Exposure to phthalates (PAEs) increases the risk of MetS, with MECPP (OR = 1.16, 95% CI: 1.04-1.29) being an example. Moreover, polychlorinated biphenyls (PCBs) (OR = 1.47, 95% CI: 1.13-1.93) and organochlorine pesticides (OCPs) (OR = 1.97, 95% CI: 1.33-2.90) showed a positive association with the MetS. This study reveals that EEDs are a risk factor for MetS, which provides new evidence for the relationship between population EEDs exposure and MetS.
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Plasticizer exposure and reproductive dysfunction: Assessing bisphenol A and phthalate esters impact on ovarian reserve in women with PCOS-associated infertility,
Patel, J., Chaudhary, H., Panchal, S. and Joshi, R., *Reproductive Toxicology*, Aug 2025, Vol. 135.

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder among women of reproductive age, frequently causing infertility. This study investigates the influence of endocrine-disrupting chemicals (EDCs) on ovarian reserve parameters in women with PCOS-related infertility. A cohort of 61 women with PCOS, aged 29.90 f 3.64 years, was recruited from Dr. Nagori's Institute for Infertility in Ahmedabad, Gujarat. Serum levels of Bisphenol A (BPA), Mono-ethylhexyl phthalate (MEHP), and Di-ethylhexyl phthalate (DEHP) were measured using high-performance liquid chromatography (HPLC). Ovarian reserve markers were assessed, including antral follicle count (AFC) and anti-M üllerian hormone (AMH) levels. Hormonal profiles and metabolic parameters were also analyzed. Correlations between EDCs and ovarian reserve markers were evaluated using Pearson correlation and regression analyses. The study found serum mean levels of BPA (77.80 f 51.82 ng/ml), MEHP (37.43 f 19.85 mu g/ml), and DEHP (5.77 f 7.21 mu g/ml).

Participants exhibited typical PCOS hormonal profiles with elevated testosterone and AMH levels, and significant insulin resistance was observed. Correlation analysis showed a positive relationship between AMH levels and AFC (r = 0.47, p = 0.01). However, no significant associations were found between EDC exposure and ovarian reserve markers. A high prevalence of adenomyosis and bilateral polycystic ovaries was noted among the participants. While metabolic and hormonal disruptions are prominent in PCOS, the direct impact of EDCs on ovarian reserve parameters appears minimal. This study highlights the necessity of addressing metabolic health and environmental exposures in managing PCOS related infertility to improve reproductive outcomes. https://doi.org/10.1016/j.reprotox.2025.108949

Brain Abnormalities in Children Exposed Prenatally to the Pesticide Chlorpyrifos, Peterson, B. S., Delavari, S., Bansal, R., Sawardekar, S., Gupte, C., Andrews, H., Hoepner, L. A., Garcia, W., Perera, F. and Rauh, V., *JAMA Neurology*, 2025.

Chlorpyrifos (CPF) is one of the most widely used insecticides throughout the world. Preclinical and clinical studies have suggested that prenatal CPF exposure is neurotoxic, but its effects on the human brain are unknown.To identify the associations of prenatal CPF exposure with brain structure, function, and metabolism in school-aged children.This prospective, longitudinal pregnancy cohort study was conducted from January 1998 to July 2015, with data analysis from February 2018 to November 2024 in a community in northern Manhattan and South Bronx, New York. Of 727 pregnant women of African American or Dominican descent in the original community cohort, 512 had CPF levels measured at delivery. Offspring 6 years and older were approached for magnetic resonance imaging (MRI) scanning.Prenatal CPF exposure.Anatomical MRI measures of cortical thickness and local white matter volumes, diffusion tensor imaging indices of tissue microstructure, MR spectroscopy indices of neuronal density, arterial spin labeling measures of regional cerebral blood flow, and cognitive performance measures. Prespecified hypotheses before data collection included CPF-related structural abnormalities in frontotemporal cortices, basal ganglia, and white matter pathways interconnecting them, and reduced neuronal density.Participants included 270 youths (123 boys and 147 girls) aged 6.0 to 14.7 years (mean [SD] age, 10.38 [1.12] years) with self-identified Dominican or African American mothers. Progressively higher prenatal CPF exposure levels associated significantly in childhood with progressively thicker frontal, temporal, and posteroinferior cortices; reduced white matter volumes in the same regions; higher fractional anisotropy and lower diffusivity in internal capsule white matter; lower regional blood flow throughout the brain; lower indices of neuronal density in deep white matter tracts; and poorer performance on fine motor (β, −0.30; t261 = −5.0; P < .001) and motor programming (β, −0.27; t261 = −4.36; P < .001) tasks.Prenatal CPF exposure was associated with altered differentiation of neuronal tissue into cortical gray and white matter, increased myelination of the internal capsule, poorer motor performance, and profoundly impaired neuronal metabolism throughout the brain. CPF is known to increase oxidative stress and inflammation and in turn impair mitochondrial functioning, neuronal development, and maturation of the oligodendrocyte precursor cells responsible for axonal myelination. These molecular and cellular effects of CPF likely account at least in part for the observed associations of CPF with poorer long-term brain and motor outcomes. https://doi.org/10.1001/jamaneurol.2025.2818

Systematic Evidence Map for the Per- and Polyfluoroalkyl Substances (PFAS) Universe. Shirke, A. a.-O., Radke, E. G., Jones, R., Allen, B. a.-O., Lin, C. a.-O., Ross, A. a.-O., Vetter, N. a.-O. X., Lemeris, C. a.-O., Hartman, P., Eftim, S. a.-O., Varghese, A. a.-O. X., Blain, R. a.-O., Hubbard, H. a.-O., Williams, A. a.-O., Thayer, K. a.-O. X. and Carlson, L. a.-O., Environmental Health Perspectives June 2025

BACKGROUND: Per- and polyfluoroalkyl substances (PFAS) are a research priority for the U.S. Environmental Protection Agency (EPA). Because PFAS include thousands of structurally diverse chemicals, there is a pressing need for identifying what data are available to assess the human health hazard of these compounds. OBJECTIVES: We used systematic evidence map (SEM) methods to summarize the available epidemiological and mammalian bioassay evidence for ∼14,735 chemicals identified as PFAS by EPA's Center for Computational Toxicology and Exposure (CCTE). This work is a continuation of our previous 2022 and 2024 SEMs that inventoried evidence on a separate set of ∼500 PFAS. The Comprehensive PFAS Dashboard includes evidence identified from our past SEMs and completed EPA assessments. METHODS: We conducted literature searches from peer-reviewed and gray literature sources to identify, screen, and inventory mammalian bioassay and epidemiological literature. A combination of manual review and machine learning software were utilized. A diverse array of potentially relevant supplemental content was also tracked, including mechanistic data, exposure-only studies, and studies informing chemical toxicokinetics and clearance. For each study meeting predefined population, exposure, comparator, and outcome (PECO) criteria, experimental design details and health endpoints evaluated were summarized in interactive web-based literature inventory visuals. Epidemiology studies and animal bioassay studies with ≥21-day exposure duration or reproductive/developmental study design proceeded to undergo a study evaluation for risk of bias and sensitivity, as well as detailed extraction of health endpoint data. Underlying data are publicly available and can be downloaded. RESULTS: Scientific database searches retrieved 152,205 references. After full-text screening, there were 347 mammalian bioassay and 44 epidemiological studies that met PECO criteria. The mammalian bioassay and epidemiological evidence assessed 99 and 30 individual PFAS, respectively (n = 18 PFAS with both). The epidemiological evidence assessed 15 health systems and the mammalian bioassay evidence assessed 16 health systems. DISCUSSION: Results from our 2022 and 2024 SEMs and completed EPA assessments are compiled into Comprehensive PFAS Dashboard. This dashboard is a resource for better understanding the currently available PFAS human health hazard data. It can be used as a tool for researchers and regulators interested in PFAS data gaps and research needs. Across all the data sources compiled into the Comprehensive PFAS Dashboard, only 1.4% (214/14,735) of PFAS had any mammalian bioassay or epidemiological data available. The vast majority of PFAS lack publicly available information about the potential human health effects of exposure to these chemicals.. https://doi.org/10.1289/EHP16952

Bisphenol A in the Urine: Association with Urinary Creatinine, Impaired Kidney Function, Use of Plastic Food and Beverage Storage Products but Not with Serum Anti-Müllerian Hormone in Ovarian Malignancies,
Sladic, M., Smrkolj, S., Kavsek, G., Imamovic-Kumalic, S., Verdenik, I. and Virant-Klun, I., *International Journal of Molecular Sciences*, May 17 2025, Vol. 26, no. 10.

Bisphenol A (BPA) is a high-production-volume industrial chemical and component of commonly used plastic products. However, it is also an endocrine-disrupting chemical that can negatively affect human health. It is not yet known whether it is associated with the development of epithelial ovarian cancer (EOC), a severe and highly fatal human disease. Therefore, the purpose of this study was to determine the concentrations of BPA in the urine of women with EOC or epithelial borderline ovarian tumors (EBOTs) using gas chromatography tandem mass spectrometry (GC-MS/MS) and find their possible associations with kidney function at the molecular level, urine and blood biochemical parameters related to metabolism, anti-M üllerian hormone (AMH) (a marker of ovarian reserve/fertility), and lifestyle habits determined via a questionnaire in comparison to healthy controls. The results suggest that the unadjusted or urine-specific-gravity-adjusted BPA levels were significantly increased in women with EOC/EBOT. The unadjusted BPA was significantly positively associated with urinary creatinine (p = 0.007) in all women with EOC/EBOT after

adjustment for age, body mass index, and pregnancy using multiple linear regression analysis. This may be related to kidney injury. However, no association was found between urinary BPA and serum AMH levels in women. Women with ovarian malignancies were more exposed to plastic products for storing foods and drinks. Some lifestyle habits, including refilling plastic bottles, correlate with higher urinary BPA levels across the entire cohort of women. When considering EOC or EBOT, it is necessary to consider the potential higher exposure of women to BPA, as reflected in their urine and lifestyle habits. https://doi.org/10.3390/ijms26104811

Exposure to persistent organic pollutants and sarcopenia: Revealing associations, mediated modifications, and potential mechanisms,
Tao, J., Zhai, J., Yang, J., Niu, Q., Hu, Y. and Yan, Y., *Ecotoxicol Environ Saf*, Aug 5 2025, Vol. 303, p. 118783.

BACKGROUND: Sarcopenia contributes significantly to the global disease burden, and identifying its risk factors is essential for prevention. However, the effects of persistent organic pollutants (POPs) on sarcopenia remain underexplored. OBJECTIVE: This study assessed the association between mixed POPs exposure and sarcopenia and explored the mediating roles of inflammation and oxidative stress, along with potential molecular targets. METHODS: A total of 2106 participants from the National Health and Nutrition Examination Survey (NHANES) were analyzed. Data included 19 POPs across four categories: polychlorinated biphenyls (PCBs), organochlorine pesticides (OCPs), per- and polyfluoroalkyl substances (PFAS), and polybrominated diphenyl ethers (PBDEs), as well as sarcopenia status and covariates. Logistic regression and restricted cubic splines assessed individual effects, while weighted quantile sum regression (WQS), Bayesian kernel machine regression (BKMR), and quantile-based g-computation examined mixed effects. Mediation analysis evaluated the roles of inflammation and oxidative stress, and network pharmacology identified potential pathways and targets. RESULTS: The WQS index for mixed POPs exposure was inversely associated with sarcopenia, with PCB146 contributing the most. In BKMR models, PFHS (PIP=0.65) was the top contributor to sarcopenia risk In separate WQS regression models, exposure to PCBs and PBDEs was significantly inversely associated with the risk of sarcopenia, with odds ratios (ORs) of 0.66 (95 % CI: 0.46, 0.96) and 0.74 (95 % CI: 0.57, 0.98), respectively. In contrast, OCP exposure showed a significant positive association with sarcopenia (OR: 1.86, 95 % CI: 1.31, 2.63). No significant association was found between PFAS exposure and sarcopenia (P > 0.05). Lower exposure showed a stronger negative effect for PCBs and PBDEs, whereas OCPs had the opposite trend. Inflammation mediated the effects of PCB187 and ppDDE, explaining 3.54 % and 2.87 %, respectively. CDKN1A, NFKBIA, CSF1R, and TFRC were key genes. CONCLUSION: Excessive OCPs was positively associated with sarcopenia, whereas PCBs, PFAS, and PBDEs showed inverse associations. CDKN1A, NFKBIA, CSF1R, and TFRC may be key targets through which POPs influence sarcopenia development. https://doi.org/10.1016/j.ecoenv.2025.118783

Elevated follicular fluid concentrations of ultraviolet filters associated with diminished ovarian reserve: A case-control study,
Tian, Y. C., Sun, J. L., Fang, Y., Li, C., Wang, C., Xin, Z. M., Wang, S. and Yang, X. K., *Environment International*, Jul 2025, Vol. 201, p. 10.

Ultraviolet filters (UVFs) are widely used in personal care products, their occurrence in the environment and potential detrimental effects on human health have raised significant concerns. This case-control study included 102 women-34 with diminished ovarian reserve (DOR) and 68 healthy controls-and aimed to investigate the association between UVF exposure and DOR. We collected and analyzed follicular fluid (FF) samples from women diagnosed with DOR and compared them to samples from a control group, measuring the concentrations of 16 different UVFs. Four

individual compounds showed significantly higher concentrations in the DOR group: octyl methoxycinnamate (OMC), UV-P, UV-328, and Ensulizole. The cumulative concentration of ten UVFs with detection frequencies above 50 % was also markedly elevated in the DOR group (median Sigma UVFs: 178.96 ng/mL vs. 23.93 ng/mL, p < 0.001). OMC exhibited the highest median concentration (170.81 ng/mL in DOR vs. 20.77 ng/mL in controls, p < 0.001), followed by UV-P, UV-328, and Ensulizole. Spearman analysis revealed significant negative correlations between OMC concentrations with ovarian reserve biomarkers such as anti-M & uuml;llerian hormone (AMH), antral follicle count (AFC), and the number of oocytes retrieved during ovarian stimulation cycles, while exhibiting a positive correlation with follicle-stimulating hormone (FSH) levels. Adjusted logistic regression models demonstrated that elevated OMC levels were associated with a 3.8-fold increased risk of DOR (95 % CI: 1.943-9.782, p < 0.001). These results highlight the urgent need for further investigation into the mechanisms by which UVFs affect ovarian reserve, as well as their potential long-term implications for fertility. https://doi.org/10.1016/j.envint.2025.109573

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

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

Poly-and perfluoroalkyl substances (PFAS) in the first 1000 days reduce linear growth, lean body mass and bone mineral density at age 3 years,
Van Beijsterveldt, I., Dorrepaal, D. J., Van Zelst, B. D., Van Den Berg, S. a. A. and Hokken-Koelega, A. C. S., *Clinical Nutrition*, Jul 2025, Vol. 50, p. 175-182.

Background and aims: Poly- and perfluoroalkyl substances (PFAS) are non-degradable, man-madechemicals. They are considered to be 'Endocrine Disrupting Chemicals' (EDCs), a group of chemicals which interfere with endocrine processes and cause adverse effects on perinatal, neurodevelopmental, metabolic and reproductive outcomes. Especially when exposure occurs during susceptible periods of development, such as early life. Infants who had exclusive breastfeeding (EBF) for at least 3 months, have persistently 3-times higher PFAS plasma levels compared to infants who had exclusive formula feeding (EFF) during the 'first 1000 days' of life. However their effects on growth and body composition outcomes are lacking. We investigated the associations between early life plasma PFAS levels and growth, body composition and metabolic

outcomes at age 3 years. Secondly, we studied if the influence of PFAS was different for EBF- and EFF-children, in order to examine if PFAS exposure through human milk diminishes the known health benefits of breastfeeding. Methods: In 237 healthy term-born infants (99 EBF, 57 EFF and 81 mix), included in Sophia Pluto birth cohort, we determined anthropometrics, blood pressure, body composition and total body bone mineral density (BMD) by Dual-energy-X-ray Absorptiometry (DXA) at age 3 years. The plasma levels of 5 PFAS were determined by liquid-chromatography-electrospray-ionization-tandem-mass-spectrometry (LCESI-MS/MS) in samples collected at age 3 months and 2 years. We studied the associations between plasma PFAS levels and outcomes at age 3 years using multiple regression models, corrected for confounders, such as feeding practices in early life. Results: Higher PFAS levels at age 3 months and 2 years were associated with less linear growth from birth until age 3 years (B: -0.068, p = 0.004 and B:-0.105, p < 0.001) and with shorter height SDS (B: -0.063, p = 0.010 and B:-0.099,p < 0.001) at age 3 years. Additionally, higher PFAS levels at age 2 years were associated with lower lean body mass (LBM) SDS and lower BMDTotalBody SDS at age 3 years (B: -0.064, p = 0.003 and B:-0.075, p = 0.018, respectively). In contrast, exclusive breastfeeding for at least 3 months was positively associated with the same outcomes (B: 0.204, p = 0.010 and B: 0.274, p = 0.019, respectively). Conclusions: Higher plasma PFAS levels in 'the first 1000 days' of life were negatively associated with height, LBM and BMD SDS at age 3 years, while exclusive breastfeeding during the first 3 months of life was positively associated with these outcomes. This suggest that early life plasma PFAS levels could jeopardize breastfeeding's known health benefits, which warrants further research. (c) 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). https://doi.org/10.1016/j.clnu.2025.05.017

Prenatal exposure to bisphenol-A and neurocognitive changes in children aged 2 to 5 years: a systematic review,
Vian Matias De Oliveira, I., Martins De Albuquerque, F., De Jesus Fernandes, A., Berti Zanella, P. and Alves Silva, M., *Rev Environ Health*, Aug 5 2025.

Bisphenol-A (BPA) is a synthetic organic compound considered an endocrine disruptor. Childhood exposure to BPA has been linked to impaired memory and learning, as well as Attention Deficit Hyperactivity Disorder. The aim of this study was to review the available literature on prenatal exposure to BPA and its relationship to the neurocognitive development of children aged 2-5 years. This systematic review (CRD42023494940 registration PROSPERO) was conducted between December 2023 and May 2024, following the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyzes (PRISMA) guidelines. The Web of Science, Embase, and PubMed databases were used for the search, with no publication date limit. The following terms, with the respective Boolean operators, were searched: ((bisphenol A) OR (BPA)) AND ((pregnancy) OR (pregnant woman)). Twenty-one longitudinal studies were selected for this review. Most studies have demonstrated negative effects of prenatal BPA exposure on the neurocognitive development of children aged 2-5 years. These results differed between the sexes, with females having lower emotional control, reduced language dominance and problem solving, and males having lower psychomotor development and higher prosocial behavior, among other differences. Overall, BPA exposure during pregnancy has been associated with hyperactivity, aggression, anxiety, depression, inattention, and sleep problems. It is concluded that maternal exposure to BPA during pregnancy results in adverse health effects in children aged 2-5 years, with impairments in their neurocognitive development. https://doi.org/10.1515/reveh-2024-0161

Early life phthalate exposure impacts gray matter and white matter volume in infants and young children,

Werder, E. J., Lu, K., Liu, C. W., Thistle, J. E., Rager, J. E., Li, G., Wu, Z. W., Li, T. F., Wang, L., Sandler, D. P., Gilmore, J. H., Piven, J., Zhu, H. T., Lin, W. L. and Engel, S. M., *Environmental Research*, Aug 15 2025, Vol. 279.

Objective: Prenatal phthalate exposure is associated with adverse neurodevelopmental outcomes, yet data on impacts of early life exposure remains limited. We investigated phthalate and replacement plasticizer exposures from 2 weeks to 7 years of age in relation to brain anatomical attributes, using serial structural magnetic resonance imaging (sMRI). Material and methods: Children were enrolled after birth into the UNC Baby Connectome Project, a longitudinal neuroimaging study (North Carolina, USA; 2017-2020). Urine samples (n = 406) were collected at each visit and analyzed for 17 phthalate and replacement plasticizer metabolites. Among 157 children contributing 369 sMRIs, we calculated metabolite-specific average exposures across each individual's urine samples and used linear mixed models to estimate longitudinal associations of log transformed, specific gravity-adjusted average metabolite concentrations with gray and white matter volume, and cortical volume, thickness, and surface area. We examined sex-specific differences in these associations. Results: Higher average metabolite concentration was associated with lower gray matter volume (MCPP: (-1.73 cm3, 95 % CI: -3.36, -0.10) and higher white matter volume (& sum;DEHP: 2.28 cm3, 95 % CI: 0.08, 4.48). Among boys (n = 72, 140 sMRIs), MEP (-2.97 cm3, 95 % CI: -5.85, -0.09) and MiBP (-2.40 cm3, 95 % CI: -4.64, -0.15) were also associated with lower gray matter volume. Among females (n = 85, 229 MRIs), higher & sum;DINCH exposure was associated with higher white matter volume (2.27 cm3, 95 % CI: 0.29, 4.25). We observed significant sex interactions for & sum;DEHP with gray matter (p-interaction = 0.03) and & sum;DINCH with white matter volume (p-interaction = 0.001). Conclusion: Early life phthalate/plasticizer exposure may differentially impact various brain region volumes in early childhood, with potential downstream consequences on functional development.
https://doi.org/10.1016/j.envres.2025.121826

Association between phthalate exposure and reproductive health in patients undergoing assisted reproductive treatment: A systematic review and meta-analysis,
Xie, G. M., Zhou, Y. J., Zheng, Q. Y., Wang, L., Wang, Y., Zeng, H. J., Wang, J. L. and Li, X. Y., *Reproductive Toxicology*, Sep 2025, Vol. 136.

This systematic review and meta-analysis synthesizes current literature examining the relationship between phthalate exposure and reproductive health in patients undergoing assisted reproductive treatment (ART). We conducted a comprehensive search across multiple databases, including PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), China Science and Technology Journal Database (VIP), and Wanfang databases. From 16 relevant publications identified, five studies were included in the systematic review and 11 in the meta-analysis. Our findings indicate that most of the 18 phthalate metabolites analyzed demonstrated negative associations with reproductive health outcomes in ART patients. High molecular weight phthalates, particularly mono (2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), were most frequently linked to adverse outcomes, followed by metabolites such as mono-isobutyl phthalate (MiBP), mono-benzyl phthalate (MBzP). Both high and low molecular weight phthalates, including monoethyl phthalate (MEP) and MiBP, were correlated with negative reproductive outcomes. However, no significant associations were observed between mono-2-ethyl-5-hydroxyhexyl terephthalate (MEHHTP) or mono-3-hydroxybutyl phthalate (MHBP) and reproductive health parameters. Our analysis suggests that phthalate exposure may adversely affect fertility, hormone levels, and gamete quality, while also being associated with pregnancy complications and oxidative stress. These findings underscore the need for further large-scale

studies to confirm these relationships and their clinical implications.
https://doi.org/10.1016/j.reprotox.2025.108948

Association of prenatal exposure to phthalates with risks of asthma, wheeze, and allergic diseases during childhood: a systematic review and meta-analysis,
Yang, J., Zhang, M., Luo, J., Pan, J., Luo, T. and Yang, W., *J Environ Health Sci Eng*, Dec 2025, Vol. 23, no. 2, p. 26.

BACKGROUND: Phthalates are one of the most common environmental contaminants and endocrine disruptors. Environmental exposure to phthalates may increase the risk for allergic diseases. However, the existing literature presents conflicting findings regarding the long-term impact of early-life exposure to these substances. METHODS: We searched the Web of Science, PubMed and Google Scholar, Medline and Embase databases for all related publications from 1974 to September 1st, 2024. Ultimately, 22 studies with a total of 16,161 participants were selected. The relative risks (RRs) with 95% confidence intervals (95% CIs) were used to evaluate whether prenatal phthalate exposure is associated with allergic endpoints. To assess statistical heterogeneity across studies, both the Q-test and I (2) statistic were adopted. Publication bias of the included studies was evaluated using Begg's and Egger's tests. Stratified analysis was conducted based on the gender of children, molecular weight of phthalates, disease type, phthalate species, parental exposure period and region. The systematic literature search protocol was formally registered in PROSPERO. RESULTS: Childhood wheeze (RR 1.10, 95% CI: 1.00-1.21), eczema (RR 1.09, 95% CI: 1.01-1.17), and rhinitis (RR 1.05, 95% CI: 1.02-1.09) are potentially associated with prenatal exposure to phthalates, particularly butyl-benzyl phthalate (RR 1.15, 95% CI: 1.06-1.24), di-ethyl-hexyl phthalate (RR 1.08, 95% CI: 1.02-1.15) and di-iso-nonyl phthalate (RR 1.12, 95% CI: 1.02-1.23). CONCLUSION: Maternal phthalate exposure during pregnancy exhibits a significant association with elevated risks of childhood respiratory and allergic manifestations, including wheezing episodes, eczematous dermatitis, and rhinitis symptoms. SUPPLEMENTARY INFORMATION: The online version contains supplementary material available at 10.1007/s40201-025-00951-3.
https://doi.org/10.1007/s40201-025-00951-3

Exposure to Dioxin-like polychlorinated biphenyls during Pregnancy and fetal thyroid function; A mixture analysis,
Yu, Y., Wu, B., Li, Z., Hu, Y., Zhang, D. and Yang, C., *Ecotoxicol Environ Saf*, Sep 1 2025, Vol. 302, p. 118646.

Despite growing evidence of the endocrine-disrupting effects of dioxin-like polychlorinated biphenyls (DL-PCBs), the specific impact of maternal exposure to these pollutants on fetal thyroid hormone levels remains largely unexplored. This study uniquely investigates the association between prenatal DL-PCB exposure and thyroid hormone levels in umbilical cord blood within a cohort of pregnant women in Shenyang, China, during 2022-2023. A total of 2240 pregnant women were enrolled in the study. Umbilical thyroid hormone levels (free thyroxine (T4), free triiodothyronine (T3), and thyroid-stimulating hormone (TSH)) were measured using electro-chemiluminescence immunoassays. 12 specific congeners of DL-PCB levels in serum samples were assessed. Linear regression models, quantile g-computation (g-comp), generalized weighted quantile sum (g-WQS) regression, and Bayesian Kernel Machine Regression (BKMR) were used to analyze the data and evaluate the effects of DL-PCBs exposure on thyroid hormone levels, adjusting for various confounders. Linear regression analysis revealed significant negative associations between several DL-PCB congeners and umbilical T4 levels, with the strongest effect observed for PCB126. PCB105 was negatively associated with umbilical T3 levels, while multiple congeners (PCB77, PCB81, PCB105, PCB169, and PCB189) were negatively associated with TSH levels. No significant

associations were found for the T4/T3 ratio. The g-comp analysis confirmed that mixture exposure to DL-PCBs was significantly associated with decreased umbilical T4 and TSH levels, with reductions seen with each one-quartile increase in exposure. However, no significant associations were observed for T3 levels or the T4/T3 ratio. The gWQS analysis did not find significant associations between DL-PCB exposure and thyroid hormones, suggesting potential sensitivity differences between mixture modeling approaches. BKMR analysis indicated a downward trend in T4 and TSH levels with increasing DL-PCB exposure, especially at lower exposure quartiles, though the wide confidence intervals suggest some uncertainty. Overall, our findings suggest that prenatal exposure to DL-PCBs may disrupt fetal thyroid function, particularly affecting T4 and TSH levels. https://doi.org/10.1016/j.ecoenv.2025.118646

Association between endocrine disrupting chemicals exposure and the risk of all-cause mortality in individuals with diabetes mellitus or its complications: A prospective cohort study,
Zhang, Y. H., Zhang, Z. L., Zhou, F. Y., Xu, G. C., Huang, W. C., Wang, M. Y., Lan, Y. Q., Zhang, W., Liu, Z. Y., Chang, S. S., Qiu, S., Qi, F. and Wei, Z. R., *Environment International*, Jun 2025, Vol. 200.

Objective To investigate the association between exposure to endocrine disrupting chemicals (EDCs) and all-cause mortality in individuals with diabetes mellitus (DM) in U.S., including those with diabetic complications. Methods This prospective cohort study included participants with DM in the 1999-2018 National Health and Nutritional Examination Survey. Data on mortality was obtained from national death records up to December 31, 2019. Cox regression, WQS regression and LASSO regression were constructed to examine the associations between EDCs and all-cause mortality in individuals with DM or its complications, adjusted for potential confounders. Restricted cubic spline analysis was used to investigate the linear relationship. Subgroup analyses were also tested in prespecified subgroups of interest. Results The study included 3,453 participants. Mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-2-ethyl-5-carboxypentyl phthalate (MECPP) showed positive associations with all-cause mortality (MEHHP: 1.14 (CI1.00-1.29); MEOHP: 1.14 (CI 1.00-1.30); MECPP: 1.17 (CI 1.00-1.37)). These also exhibited positive associations with all-cause mortality in the participants with diabetic kidney disease (MEHHP: 1.24 (CI 1.08-1.42); MEOHP: 1.27 (CI 1.10-1.47); MECPP: 1.43 (CI 1.19-1.71)). Bisphenol A 1.45 (1.08, 1.96) and MCPP 1.59 (CI 1.24-2.05) showed positive associations with all-cause mortality in the diabetic retinopathy (DR) participants. MEHHP exposure interacted with hypertension in DM and hypercholesterolemia, as well as with age in DR populations. MCPP exposure interacted with age in DR, significantly amplifying mortality risks (P interaction < 0.05). Conclusions This study provided epidemiological evidence that higher concentrations of certain EDCs are associated with an increased risk of all-cause mortality in participants with DM or its complications. https://doi.org/10.1016/j.envint.2025.109556

The causal role of endocrine disrupting chemicals in pubertal timing: a Mendelian randomization study,
Zuo, M., Gamache, I., Fagbemi, K., Day, F. R., Ong, K. K. and Manousaki, D., *Journal of Pediatric Endocrinology & Metabolism*, Jul 28 2025, Vol. 38, no. 7, p. 753-760.

Objectives Endocrine disrupting chemicals (EDCs) interfere with hormonal homeostasis, and have been observationally linked to altered pubertal timing, defined by the age of menarche (AAM) in girls and the age at voice change (AVC) in boys. However, the causality of these associations remains unclear. We used Mendelian randomization (MR) to investigate if genetically altered serum EDC levels affect pubertal timing.Methods We performed univariate MR to assess the effects of 22 EDCs on AAM and AVC, using the largest GWAS for EDCs as well as European and multi-ethnic GWAS on AAM and AVC. Multivariate MR (MVMR) and two-step MR were conducted to examine

mediating effects of body mass index (BMI).Results We found causal MR associations with AAM for three polychlorinated biphenyls (PCBs): PCB 74 (beta IVW: -0.015, 95 % CI [-0.028, -0.003], p=0.014), PCB 194 (beta IVW: -0.015, 95 % CI [-0.024, -0.007], p=3.27x10-4), and PCB 206 (beta IVW: -0.024, 95 % CI [-0.041, -0.006], p=0.0068) and for dibutyl phthalate (DBP, beta IVW: 0.006, 95 % CI [0.001, 0.010], p=0.013). One MR association was found with AVC for bisphenol A (BPA, beta Wald ratio= -0.032, 95 % CI [-0.044, -0.019], p=2.62x10-7). Mediation analyses by MVMR or Two-Step MR suggested BMI's mediating role in the associations of EDCs with AAM and AVC.Conclusions Our findings indicate that exposure to specific PCBs leads to earlier AAM whereas exposure to DBP delays AAM. Exposure to BPA leads to earlier AVC, with BMI potentially acting as a mediator.
https://doi.org/10.1515/jpem-2025-0146

Toxicité sur l'homme

Redefining the pathogenesis of Gestational Diabetes Mellitus: The cumulative impact of endocrine disrupting environmental chemicals in key metabolic pathways,
Aayush, M. V., Nikthesh, G., Rajmohan, D., Ravindran, C. P., Vasantharekha, R., Thangavelu, S. and Seetharaman, B., *Medical Hypotheses*, Aug 2025, Vol. 201.

Gestational Diabetes Mellitus (GDM) is a common pregnancy complication with a prevalence rate of 10-14 % in India. In GDM high blood glucose level and insulin resistance is observed. Several hormones secreted from placenta during pregnancy changes the metabolic state and interferes with insulin functions and blocks insulin and increases blood glucose level/hyperglycemia. Emerging evidence links GDM to environmental exposures, particularly endocrine-disrupting chemicals (EDCs) such as Bisphenol A (BPA), phthalates, parabens, and microplastics. These EDCs impair glucose metabolism and insulin signaling through oxidative stress, inflammation, hormonal interference, and pathway disruptions, including the hypothalamic-pituitary-thyroid (HPT) axis and PI3K-AKT signaling. This paper hypothesizes that frequent EDC exposure in pregnant women might trigger HPT axis thereby increasing insulin resistance and impair glucose homeostasis increasing the risk of GDM. Supporting evidence from mechanistic and epidemiological studies highlights the need for regulatory policies and early detection strategies. Validating this hypothesis could reshape GDM prevention and management by identifying therapeutic targets and minimizing EDC exposure.
https://doi.org/10.1016/j.mehy.2025.111693

RNA-Seq Uncovers Association of Endocrine-Disrupting Chemicals with Hub Genes and Transcription Factors in Aggressive Prostate Cancer,
Alwadi, D., Felty, Q., Doke, M., Roy, D., Yoo, C. and Deoraj, A., *International Journal of Molecular Sciences*, Jun 6 2025, Vol. 26, no. 12.

This study analyzes publicly available RNA-seq data to comprehensively include the complex heterogeneity of prostate cancer (PCa) etiology. It combines prostate and prostate cancer (PCa) cell lines, representing primary PCa cells, Gleason scores, ages, and PCa of different racial origins. Additionally, some cell lines were exposed to endocrine-disrupting chemicals (EDCs). The research aims to identify hub genes and transcription factors (TFs) of the prostate carcinogenesis pathway as molecular targets for clinical investigations to elucidate EDC-induced aggressiveness and to develop potential biomarkers for their exposure risk assessments. PCa cells rely on androgen receptor (AR)-mediated signaling to survive, develop, and function. Fifteen various RNA-seq datasets were normalized for distribution, and the significance (p-value < 0.05) threshold of differentially expressed genes (DEGs) was set based on |log2FC| >= 2 change. Through integrated bioinformatics, we applied cBioPortal, UCSC-Xena, TIMER2.0, and TRRUST platforms, among others, to associate

hub genes and their TFs based on their biologically meaningful roles in aggressive prostate carcinogenesis. Among all RNA-Seq datasets, we found 75 overlapping DEGs, with BUB1B (32%) and CCNB1 (29%) genes exhibiting the highest degree of mutation, amplification, and deletion. EDC-associated CCNB1, BUB1B, and CCNA2 in PCa cells exposed to EDCs were consistently shown to be associated with high Gleason scores (>= 4 + 3) and in the >60 age group of patients. Selected TFs (E2F4, MYC, and YBX1) were also significantly associated with DEGs (NCAPG, MKI67, CCNA2, CCNB1, CDK1, CCNB2, AURKA, UBE2C, BUB1B) and influenced the overall survival (p-value < 0.05) of PCa cases. This is one of the first comprehensive studies combining 15 publicly available RNA-seq datasets to demonstrate the association of EDC-associated hub genes and their TFs aligning with the aggressive carcinogenic pathways in the higher age group (>60 years) of patients. The findings highlight the potential of these hub genes as candidates for further studies to develop molecular biomarkers for assessing the EDC-related PCa risk, diagnosing PCa aggressiveness, and identifying therapeutic targets. https://doi.org/10.3390/ijms26125463

Non-occupational exposure to cadmium and breast cancer: A comprehensive and critical review, Anicic, R., Zekovic, M., Kocic, M., Gluvic, Z., Manojlovic, D., Scancar, J. and Stojsavljevic, A., *Ecotoxicology and Environmental Safety*, Jun 15 2025, Vol. 298.

Breast cancer (BC) is a multifactorial disease with unresolved etiology. Environmental pollutants, primarily trace metals, play a pivotal role in the pathophysiological cascade of malignant tumors, including BC. In this up-todate review, we comprehensively and critically examined the relationship between cadmium (Cd) and BC. For this purpose, peer-reviewed studies from relevant databases (PubMed, SCOPUS, and Cochrane Library) over the last 40 years were retrieved and analyzed. We found that in vitro and in vivo studies strongly support the view that Cd has harmful effects on breast health. According to the human studies, we found that Cd could be responsible for the development and progression of malignant breast tumors due to markedly higher levels in clinical matrices of cases (whole blood, urine, breast tissue, keratin materials) than in clinical matrices of controls. Cadmium does not appear to affect BC density. In contrast, Cd has been found to have a detrimental effect on sex hormones, disrupting the balance of estrogen and androgen. We found that studies looking at dietary Cd intake and BC risk generally (without measuring urine or blood Cd) do not support the association between dietary Cd intake and BC risk. In notable contrast, studies looking at dietary Cd intake and BC risk by measuring Cd in urine or blood generally support this association. The effect of airborne Cd on BC risk was weak, but in favor of specific histological forms, primarily ER-/PR- invasive tubular breast carcinomas. Regardless of the intake route of Cd into the body, it can be concluded that Cd has a harmful effect on breast health. However, well-designed longitudinal, mechanistic, meta-analytic, and other studies are urgently needed to confirm the exact role of environmental Cd in breast carcinogenesis. https://doi.org/10.1016/j.ecoenv.2025.118331

Can Bisphenols Alter the Inflammation Process?, Bazany, D., Greifova, H., Zuscikova, L., Tokarova, K., Jambor, T., Kovacik, A. and Lukac, N., *Life-Basel*, May 14 2025, Vol. 15, no. 5.

This review's main purpose is to draw attention to the possible influence of widely used bisphenols on the inflammatory process. Bisphenols are endocrine-disrupting chemicals that are produced worldwide in great quantities. From this point of view, it is very important to clarify their influence on innate immune reactions, which protect the integrity of the body against the action of various pathogens on a daily basis. The inflammation process consists of several key factors that are produced at different levels of this reaction. Each of these levels can be affected by endocrine disruptors, from the point of view of modifying either the immune system cells that intervene in this process or the way in which they produce inflammatory mediators. The development of new

recommendations for the use of bisphenols is a complex issue given their influence on inflammatory processes. Because the immune system and immune response are so intricate, bisphenols may pose more risk to humans than is presently recognized. This paper discusses the classification of bisphenols, the fundamental mechanism of inflammation, the characterization of inflammatory mediators, and the current knowledge of the molecular mechanisms behind the impact of bisphenols on the inflammatory response. https://doi.org/10.3390/life15050782

Bisphenol A drives nuclear factor-kappa B signaling activation and enhanced motility in non-transformed breast cells,
Citarella, A., Besharat, Z. M., Coppola, L., Sabato, C., Autilio, T. M., Vicentini, E., Bimonte, V. M., Catanzaro, G., Pediconi, N., Fabi, A., Migliaccio, S., Milella, M., Bei, R. B. R., Ferretti, E. and Po, A. G. S., *Environmental Pollution*, Jul 1 2025, Vol. 376.

Bisphenol A (BPA) is a chemical compound found in a wide range of everyday consumer products, resulting in human exposure. BPA has been described as an endocrine disruptor, affecting different systems of the human body. Notably, nanomolar levels of BPA have been detected in human matrices, including plasma and milk. BPA exposure has been associated with the development of breast cancer, and the increase in breast cancer incidence prompted us to investigate the effects of BPA in MCF10A, a model of non-transformed mammary epithelium. Cells were treated with 10 nM BPA for 24 h to capture early molecular alterations preceding phenotypic transitions. Comprehensive transcriptomic analyses were conducted to identify differentially expressed genes and enriched signaling pathways. Subsequent validations included assessment of cytokine release, protein expression, immunofluorescence for subcellular localization of Nuclear Factor-Kappa B (NF-kappa B), and evaluation of actin cytoskeletal organization. Transcriptome analysis revealed enrichment in interleukin signaling and activation of the NF-kappa B pathway following BPA exposure. Functional assays demonstrated that BPA treatment enhanced cell motility, accompanied by increased phosphorylation of NF-kappa B. Inhibition of NF-kappa B effectively mitigated BPA-induced effects, including augmented cell motility, nuclear translocation of NF-kappa B, and cytoskeletal rearrangements. Notably, inhibition of the Mitogen-Activated Protein Kinase (MAPK) pathway, and to a lesser extent of the AKT pathway, counteracted BPA-induced NF-kappa B activation and the associated increase in cell motility. In conclusion, we show that nanomolar concentration of BPA induces significant changes in the molecular setting and behaviour of non-tranformed breast cells, activating NF-kappa B signalling that in turn controls inflammation, cell cycle, proliferation and cell motility. Our findings indicate that nanomolar concentrations of BPA can induce significant molecular and behavioral changes in non-transformed breast epithelial cells. These results contribute to a deeper understanding of how environmental pollutants like BPA may perturb breast epithelial cell function and potentially contribute to carcinogenesis.
https://doi.org/10.1016/j.envpol.2025.126422

Étude de l'influence des polluants environnementaux sur l'incidence du diabète de type 2. Thèse présentée en vue de l'obtention du grade de Doctorat en Sciences Biomédicales et Pharmaceutiques,
Claessens, J., *Université de Liège* (2025),
L'objectif de notre travail est de contribuer à la compréhension du lien potentiel entre la pollution chimique et le diabète de type 2. Dans un premier temps, nos recherches bibliographiques ont pointé que de nombreuses substances incriminées pour leur lien potentiel avec le diabète de type 2 sont des composés dont la demi-vie biologique est courte. Ces composés, qualifiés de polluants non persistants, sont habituellement mesurés dans l'urine mais la mesure de leurs concentrations dans les échantillons urinaires ne permet pas d'établir la contamination chronique pour ce type de composés. Pour pallier cette limitation, nous avons investigué l'utilisation du cheveu comme matrice

pour le monitoring des polluants environnementaux. Nous avons validé une méthode d'analyse de 13 polluants environnementaux (trois parabènes, deux bisphénols et huit composés perfluorés). Nous avons ensuite réalisé un biomonitoring de ces composés dans les cheveux de 114 individus vivant en Province de Liège. Ce travail nous a permis de mettre en évidence la présence des trois parabènes, des deux bisphénols et du PFOA dans 46,4 % à 97,4 % des échantillons. Afin de comprendre quelles informations sont effectivement fournies par les cheveux, nous avons ensuite comparé les niveaux de contamination de différents polluants chimiques dans le cheveu et le sérum pour huit PFAS et six PCB et dans l'urine et le cheveu pour trois parabènes et deux bisphénols. Cette étude nous a permis de mettre en évidence que de nombreux paramètres autres que la concentration ou le temps de contact influencent l'absorption des composés chimiques dans le cheveu et que les informations fournies par le cheveu et les autres matrices sont différentes. https://orbi.uliege.be/bitstream/2268/335437/1/These%20VF%20Julien%20Claessens%20.pdf

Obesity and obesity related disease in adulthood: the dark side of early life exposure to Environmental Chemical Disruptors,
Di Lorenzo, M., Aurino, L., Lonardo, M. S., Cacciapuoti, N., Nasti, G., Belfiore, A., Guida, B. and Chiurazzi, M., *Journal of Endocrinological Investigation*, 2025.

PurposeThe present review aims to summarize and collect data in support of the obesogenic theory to broaden knowledge regarding the intriguing relationship between exposure to environmental chemical disruptors (EDCs), obesity and obesity related diseases.MethodsA comprehensive search of the literature from 1990 to 2024 was performed in Pubmed using the word endocrine disruptor chemicals or obesogens and: adipose tissue, metabolic diseases, weight gain, gut microbiota.ResultsIn the past, genetic factors, an unbalanced diet and a sedentary lifestyle were considered the only risk factors for obesity development. On the other hand, recent studies described the obesogenic theory, suggesting that an interaction between exposure to EDCs with obesogenic activity, especially during early life development, and the endocrine system can play a key role in the greater susceptibility to the onset of obesity, not even excluding the involvement of the gut microbiota and its alterations.ConclusionsData collected show that there is a close link between environmental exposure to EDCs during early life of development and the onset of obesity and related dysmetabolic diseases that may occur later in life. https://doi.org/10.1007/s40618-025-02620-6

Intergenerational and transgenerational effects of endocrine-disrupting chemicals in the offspring brain development and behavior,
Dias, G. R. M., Giusti, F. C. V., De Novais, C. O., De Oliveira, M. a. L., Paiva, A. G., Kalil-Cutti, B., Mahoney, M. M. and Graceli, J. B., *Frontiers in Endocrinology*, May 21 2025, Vol. 16.

Endocrine-disrupting chemicals (EDCs) are a group of substances that can alter normal body functioning by disrupting the various patterns of hormone secretion and action. Some of these substances are used as plasticizers (e.g., bisphenols and phthalates) and agrochemicals (e.g., vinclozolin). EDC exposure can occur by many routes, including oral by contaminated food and water, through the skin, inhalation, and by placental transfer from mother to fetus or mother to infant (via lactation). The increase in EDCs used by the industry has strongly impacted our health. An increasing number of scientific works have reported the effects of EDCs on cancer development, metabolism, heart disease, and fertility. Most recently, studies on EDCs effects on behavior and the developing brain are raising major concerns related to the formation of sex differences and to the increased prevalence of neuropsychiatric disorders. In this review, we highlight the recent findings of the effects of pre-, peri-, and postnatal exposure to the three well-studied EDCs (i.e., bisphenols (BPA, BPS, BPF, and BPAF), phthalates (DBP, BBP, DEHP, and DiPeP), and vinclozolin (VIN)) on

developing brain and behavior across generations in experimental animals. https://doi.org/10.3389/fendo.2025.1571689

Ultra-Processed Diets and Endocrine Disruption, Explanation of Missing Link in Rising Cancer Incidence Among Young Adults,
Fajkic, A., Lepara, O., Jahic, R., Hadzovic-Dzuvo, A., Belancic, A., Chupin, A., Pavkovic, D. and Sher, E. K., *Cancers*, Jun 29 2025, Vol. 17, no. 13.

The global increase in early-onset cancers among adolescents and young adults has happened at the same time as the rise in the consumption of ultra-processed foods (UPFs). Far beyond their poor nutritional quality, UPFs are increasingly seen as Trojan horses, complex biological agents that interfere with many functions of the human organism. In this review, we utilise the Trojan horse model to explain the quiet and building health risks from UPFs as foods that seem harmless, convenient, and affordable while secretly delivering endocrine-disrupting chemicals (EDCs), causing chronic low-grade inflammation, altering the microbiome, and producing epigenetic alterations. We bring together new proof showing that UPFs mess up hormonal signals, harm the body's ability to fight off harmful germs, lead to an imbalance of microbes, and cause detrimental changes linked to cancer. Important components, such as bisphenols and phthalates, can migrate from containers into food, while additional ingredients and effects from cooking disrupt the normal balance of cells. These exposures are especially harmful during vulnerable developmental periods and may lay the groundwork for disease many years later. The Trojan horse model illustrates the hidden nature of UPF-related damage, not through a sudden toxin but via chronic dysregulation of metabolic, hormonal, and genetic control. This model changes focus from usual diet worries to a bigger-picture view of UPFs as causes of life-disrupting damage. Ultimately, this review aims to identify gaps in current knowledge and epidemiological approaches and highlight the need for multi-omics, long-term studies and personalised nutrition plans to assess and reduce the cancer risk associated with UPFs. Recognising UPFs as a silent disruptor is crucial in shaping public health policies and cancer prevention programs targeting younger people. https://doi.org/10.3390/cancers17132196

Shared molecular mechanisms of bisphenol A and phthalates in endometriosis: A bioinformatics and molecular docking study,
Fan, Z. X., Maisaidi, R., Reheman, Y., Li, Y., Zhou, P. L. and Han, L. L., *Ecotoxicology and Environmental Safety*, Jul 1 2025, Vol. 299.

Objective: Emerging evidence links endometriosis with co-exposure to Bisphenol A (BPA) and phthalates; however, their combined toxicogenomic mechanisms remain unclear. This study investigated the shared molecular pathways of BPA and phthalates-Diethyl phthalate (DEP), Dimethyl phthalate (DMP), and Dioctyl phthalate (DOP)-in endometriosis pathogenesis. Methods: Bioinformatics and molecular docking analyses were integrated to characterize the chemical-pathway interactions in endometriosis development. Results: We identified 81 shared targets of BPA/phthalates associated with endometriosis. Functional enrichment revealed their involvement in estrogen signaling, oxidative stress, inflammation, and cell proliferation/migration. PPI network analysis prioritized four hub targets (HSP90AA1, AKT1, SRC, IGF1) validated in endometriotic lesions and functionally linked to PI3K-Akt signaling and a dual hyperinflammatory-immunosuppressive imbalance. Molecular docking demonstrated that BPA and phthalates bind these proteins at shared sites, suggesting mechanistic convergence. Conclusion: BPA and phthalates co-promote endometriosis through overlapping signaling pathways. These findings provide mechanistic insights into their combined effects and establish a framework for understanding environmental chemical synergism in disease etiology. https://doi.org/10.1016/j.ecoenv.2025.118388

Mechanisms of di (2-Ethylhexyl) Phthalate-Induced Lipid Metabolism Disorders: A Review, Fang, X., Wang, T., Lou, S., Qiao, Y., Zhang, B. and Zhou, L., *J Appl Toxicol*, Jul 28 2025.

Di(2-ethylhexyl) phthalate (DEHP) is a widely used plasticizer that can be absorbed by the human body through various pathways. Numerous studies have indicated the adverse effects of DEHP on lipid metabolism. Experimental and population studies have provided evidence for DEHP-induced lipid metabolism disorder. This review discusses the cellular pathophysiological changes leading to lipid metabolism disorders, including inflammation, apoptosis, autophagy, and oxidative stress. We also summarize the key molecules and signaling pathways involved in the lipid metabolism disorder induced by DEHP. Additionally, multiple omics such as metabolomics, transcriptomics, and epigenetics are discussed in this review. Furthermore, this article provides some directions for future research about the mechanisms of lipid metabolism disorders caused by DEHP, aiming to offer more detailed and reliable theoretical evidence for the prevention and treatment of lipid metabolism disorders. https://doi.org/10.1002/jat.4867

The effect of phthalates on insulin secretion of pancreatic beta cells based on cellular studies, a systematic review,
Ghanati, K., Pourjafar, H., Shavali-Gilani, P., Akbari, N., Tavoosidana, G., Zandsalimi, F., Abdolhosseini, M., Aghaei, M. and Sadighara, P., *Toxicology Letters*, Jul 2025, Vol. 410, p. 76-82.

Diabetes is increasing worldwide. Phthalates are regularly detected in food and ecosystem environments at detectable levels. The purpose of this study was to review and summarize the effect of phthalates on insulin secretion from pancreatic B-cell. Also, the toxicity of pancreatic B-cell caused by phthalates and the mechanism of toxicity were discussed in detail. To evaluate the amount of insulin secretion, the cells are usually exposed to two different concentrations of glucose (high and low). In almost all phthalate concentrations at high glucose concentrations, it leads to a decrease in insulin secretion. Furthermore, the most important mechanism in the physiological changes of pancreatic B-cell was assigned to oxidative stress. The relationship between insulin secretion and oxidative stress parameters with phthalate concentration was identified in all studies. As phthalate concentrations increase, decreased insulin secretion and increased oxidative stress damage are observed in pancreatic beta cells. https://doi.org/10.1016/j.toxlet.2025.06.002

Liver Toxicity Induced by Exposure to Bisphenol Analogs at Environmentally Relevant Levels: Insights from a Literature Review on Multiple Species,
Guo, T. L., Eldefrawy, F. and Guo, K. M., *Livers*, May 27 2025, Vol. 5, no. 2.

Bisphenol analogs and their derivatives have been identified in human tissue and our living environment. There are major concerns over exposure to bisphenol analogs, especially the low-dose- and mixture-related toxicities, as they are considered potential endocrine-disrupting chemicals that may cause adverse effects in multiple organ systems. The liver is a critical organ responsible for an array of functions, e.g., metabolism, immunity, digestion, detoxification and vitamin storage, in addition to being a leading chemical target site. In this literature review of multiple species, we discussed the metabolism of bisphenol analogs in the liver, which was followed by discussions of bisphenol analog-induced liver toxicity in various species, including humans, rodents (mice and rats) and other species (chicken, pig, sheep, etc.). Further, the mechanisms of action and markers of liver damage such as oxidative stress, apoptosis, inflammation and fibrosis were discussed. It was concluded that bisphenol analogs can produce toxic effects on the liver in different species through various mechanisms, including epigenetic modifications and disruptions of the cell signaling pathways, gene expression, microbiome and metabolome. More research should be conducted to study the toxicity of bisphenol analogs other than bisphenol A and the underlying mechanisms of

action, and in particular the potential for causing dysbiosis. Understanding the mechanisms of liver injury holds promise for improving the prediction of liver toxicity from bisphenol analogs and other environmental chemicals, and their risk assessment and legislation.
https://doi.org/10.3390/livers5020024

The Presence of Microplastics in Human Semen and Their Associations with Semen Quality, Guo, Y., Rong, M., Fan, Y., Teng, X., Jin, L. and Zhao, Y., *Toxics*, Jul 3 2025, Vol. 13, no. 7.

Microplastics (MPs) are becoming one of the most serious environmental threats worldwide. They have been shown to induce male reproductive toxicity in animal studies. However, evidence of their adverse effects on male reproductive health in human is still lacking. In this study, we evaluated the presence of MPs in human semen and explored their associations with semen quality. A total of 45 semen samples from men attending a fertility center were collected. MPs in the semen samples were analyzed by laser direct infrared (LD-IR) spectroscopy. MPs were found in 34 out of 45 semen samples, with an average abundance of 17.0 (42.0) particles/g. The size of MPs ranged from 20.3 µm to 189.7 µm and the majority (57.8%) were smaller than 50 µm. A total of 15 distinct MPs polymers were identified, and polyethylene (PET) accounted for 35.9% of the total amount of MPs, followed by butadiene rubber (BR, 26.4%) and chlorinated polyethylene (CPE, 12.2%). Analysis of the association of MP exposure with semen quality showed that participants exposed to PET MPs experienced a reduction in sperm progressive motility (20.6% ± 12.8% vs. 34.9% ± 15.9%, p = 0.056). However, no significant association was found between MP exposure and sperm concentration or total sperm count. Our findings confirmed the presence of MPs in human semen and suggested that MP exposure might have adverse impacts on male reproductive health. However, further large-scale studies are needed to confirm these findings. https://doi.org/10.3390/toxics13070566

Integrative causal and single-cell analyses reveal genes responsive to endocrine disruptors driving human male infertility,
Hong, Y., Wang, Y., Li, J., Shu, W., Chen, H. and Chen, C., *Ecotoxicol Environ Saf*, Sep 1 2025, Vol. 302, p. 118709.

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

Integrative causal inference illuminates gene-environment interactions linking endocrine disruptors to female infertility,
Hong, Y. G., Du, Z. Y., Li, J. J., Wang, Y., Wang, Y. R., Shu, W. Y., Shen, Q. X., Chen, F. and Li, S. S., *Ecotoxicology and Environmental Safety*, Sep 1 2025, Vol. 302.

Female infertility, a global health concern affecting up to 12 % of women, is influenced by genetic, hormonal, and environmental factors. Among environmental contributors, endocrine-disrupting chemicals (EDCs), which interfere with hormonal systems, have gained attention for their potential impact on reproductive health. This study used Mendelian randomization (MR) and colocalization analyses to explore the causal relationships between gene expression influenced by EDCs and female infertility. We identified 4207 EDC-related genes from The Endocrine Disruption Exchange (TEDX) database and Comparative Toxicogenomics Database (CTD), and analyzed their potential causal effects on female infertility using genome-wide association data. A total of five genes showed significant associations with infertility risk, with SULT1B1, MASTL, and TTC39C linked to increased risk, and ESR1 and AKAP13 associated with a protective effect. Colocalization analysis revealed that four of these genes (ESR1, TTC39C, AKAP13, and SULT1B1) shared causal variants with infertility, strengthening the MR findings. Additionally, interactions between these genes and key EDCs like bisphenol A (BPA), tetrachlorodibenzodioxin (TCDD), and sodium arsenite highlighted complex molecular mechanisms through which environmental exposures influence fertility. These findings provide new insights into the gene-environment interactions contributing to female infertility and offer potential targets for interventions to mitigate the harmful effects of EDCs on reproductive health. https://doi.org/10.1016/j.ecoenv.2025.118679

Per-and polyfluoroalkyl substances (PFAS) in milk and dairy products: a literature review of the occurrence, contamination sources, and health risks,
Hossini, H., Massahi, T., Parnoon, K. and Nouri, M., *Food Addit Contam Part A Chem Anal Control Expo Risk Assess*, Jul 28 2025, p. 1-13.

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

Human endocrine disruption: an updated review of toxicological insights into parabens and phthalates,
Isaac, R. a. A., Subbarayalu, R., Kumar, M. S. K., Martin, T. M., Lo, S. C. and Santosh, W., *Toxicology and Environmental Health Sciences*, 2025.

Every day, humans are exposed to a wide range of chemicals from numerous sources. A variety of contaminants are released into the environment through the use of personal care products (PCPs). In recent years, various types of beauty care products have been introduced, and their usage has significantly increased. Although the concentrations of harmful chemicals in PCPs are minimal, they can have adverse effects on human health and well-being. These chemicals primarily affect the endocrine system and may impair human reproductive success. Parabens and phthalates are common endocrine-disrupting chemicals present in PCPs used daily. Several previous studies have reported the harmful effects of parabens and phthalates, such as disruptions in thyroid gland secretion, sperm production, and reproductive hormone secretion, causing infertility, carcinogenesis, and pregnancy-related complications. Conversely, other studies have found either no significant effects or only negligible impacts on the human endocrine system. Therefore, in this review, we examine the harmful effects of parabens and phthalates on the human endocrine system by analyzing updated findings from various in vitro and in vivo studies. Di(2-ethylhexyl) phthalate has been associated with endometriosis, intrauterine growth retardation, fibromyoma, and pregnancy loss. Similarly, butyl paraben has been shown to reduce sperm concentration and sperm count; methyl paraben to impair poor sperm motility; and propyl paraben to alter follicle-stimulating hormone concentration. Furthermore, it has been observed that the effects of parabens and phthalates are more pronounced in animals than in humans primarily due to higher dosages administered during in vivo studies. In summary, the toxic effects of parabens and phthalates on the human endocrine system depend largely on dosage, geographical location, lifestyle factors, and duration of exposure. https://doi.org/10.1007/s13530-025-00264-w

Exploring the relationship between the androgen receptor and structural configuration of benzophenones: a combination of computational analysis and laboratory models,
Jeong, D., Pathak, R. K., Jung, D. W., Kim, J. M. and Lee, H. S., *Environment International*, Aug 2025, Vol. 202.

This study explored the interactions between benzophenones (BPs) and androgen receptors (AR) using computational and experimental approaches. BPs are potential endocrine disruptors that are commonly found in cosmetics, such as sunscreen. Molecular docking and molecular mechanics with generalized Born and surface area continuum solvation calculations revealed that dihydroxylation form of BP-1, BP-2 had higher binding affinities to AR compared with BP-1, BP-3. Key interactions with residues, such as Gln711 and Asn705, were identified. Density functional theory analysis revealed that BP-2 has a balanced energy gap, which contributes to its stability and reactivity. Cell-based assays validated these computational results, showing that BP-2 had stronger AR antagonistic effect than BP-1 and BP-3. Furthermore, BP-2 enhances the AR-mediated luciferase signal at specific concentration through inducing dimerization of cytosolic AR, whereas BP-1 and BP-3 had no AR agonistic effects. These changes in AR-mediated transcriptional activation activity were observed in flutamide and hydroxyflutamide as well. As expected, changes in AR-mediated endocrine disrupting potential due to configurational modification of BP-1 to BP-2 by dihydroxylation resulted in whole AR protein expression. These findings suggest that BP-2 is a strong AR modulator and a potential endocrine disruptor, offering insights into how similar compounds may interact with AR. https://doi.org/10.1016/j.envint.2025.109632

Exploring the Role of Bifenthrin in Recurrent Implantation Failure and Pregnancy Loss Through Network Toxicology and Molecular Docking,
Jiang, S. Y., Wang, Y. X., Chen, H. Y., Teng, Y. Y., Zhu, Q. Y. and Xie, K. P., *Toxics*, May 29 2025, Vol. 13, no. 6.

Bifenthrin (BF) is a widely used pyrethroid pesticide recognized as an endocrine-disrupting chemical (EDC). Previous studies have confirmed that chronic exposure to BF is associated with various health risks. However, its potential association with recurrent implantation failure (RIF) and recurrent pregnancy loss (RPL) remains unclear. In this study, the potential targets of BF were identified using several databases, including the Comparative Toxicogenomics Database (CTD), TargetNet, GeneCards, SwissTargetPrediction, and STITCH. Differentially expressed genes (DEGs) associated with RIF were obtained from bulk RNA-seq datasets in the GEO database. Candidate targets were identified by intersecting the predicted BF-related targets with the RIF-associated DEGs, followed by functional enrichment analysis using the DAVID and g:Profiler platforms. Subsequently, hub genes were identified based on the STRING database and Cytoscape. A diagnostic model was then constructed based on these hub genes in the RIF cohort and validated in an independent recurrent pregnancy loss (RPL) cohort. Additionally, we performed single-cell type distribution analysis and immune infiltration profiling based on single-cell RNA-seq and bulk RNA-seq data, respectively. Molecular docking analysis using AutoDock Vina was conducted to evaluate the binding affinity between BF and the four hub proteins, as well as several hormone-related receptors. Functional enrichment results indicated that the candidate genes were mainly involved in apoptotic and oxidative stress-related pathways. Ultimately, four hub genes-BCL2, HMOX1, CYCS, and PTGS2-were identified. The diagnostic model based on these genes exhibited good predictive performance in the RIF cohort and was successfully validated in the RPL cohort. Single-cell transcriptomic analysis revealed a significant increase in the proportion of myeloid cells in RPL patients, while immune infiltration analysis showed a consistent downregulation of M2 macrophages in both RIF and RPL. Moreover, molecular docking analysis revealed that BF exhibited high binding affinity to all four hub proteins and demonstrated strong binding potential with multiple hormone receptors, particularly pregnane X receptor (PXR), estrogen receptor alpha (ESR alpha), and thyroid hormone receptors (TR). In conclusion, the association of BF with four hub genes and multiple hormone receptors suggests a potential link to immune and endocrine dysregulation observed in RIF and RPL. However, in vivo and in vitro experimental evidence is currently lacking, and further studies are needed to elucidate the mechanisms by which BF may contribute to RIF and RPL.
https://doi.org/10.3390/toxics13060454

Polyethylene and Polyvinyl Chloride Nanoplastics in Human Follicular Fluid and Seminal Plasma: Impact on Fertilization and Sperm Quality,
Kong, F., Fang, L., Gui, Y., Lan, H., Zhao, P., Zhang, Y., Jiang, L., Zhang, S. and Tong, X., *ACS Nano*, Aug 5 2025, Vol. 19, no. 30, p. 27159-27172.

Plastic pollution is a growing global issue, with nanoplastics (NPs) posing a greater threat than microplastics. Micro/nanoplastics have been detected in various human tissues and bodily fluids, but their impacts on human fertility remain unclear. We used pyrolysis gas chromatography-mass spectrometry (Py-GC/MS) with liquid extraction to detect NPs in the follicular fluid (FF) and seminal plasma (SP) of 51 couples undergoing in vitro fertilization (IVF) to investigate the impact of NPs on fertility. In our study, polyethylene (PE) and polyvinyl chloride (PVC) were the most frequently detected NPs. In FF, the average PE and PVC concentrations were 1.21 μg/g and 1.85 μg/g, respectively, whereas in SP, they were 3.02 μg/g and 2.67 μg/g, respectively. For NPs in FF, no significant association was detected between PE or PVC levels and the ovarian reserve, whereas IVF data indicated that higher PE concentrations in the T2 and T3 groups were associated with significantly lower fertilization rates than those in the low-concentration T1 group ($p = 0.0003$, $p = 0.007$, respectively), a trend similar to that observed for PVC ($p = 0.009$, $p = 0.008$, respectively). For the NPs in SP, the PVC concentration was associated with reduced sperm motility (p-trend = 0.044), whereas no significant difference was observed among the PE or PVC groups according to the IVF data. Neither maternal nor paternal levels of NPs were significantly associated with embryo

implantation or clinical pregnancy. In conclusion, these results indicate that NPs are detectable in both FF and SP, with PE and PVC nanoparticles adversely affecting fertilization rates and sperm quality. https://doi.org/10.1021/acsnano.5c00918

Epidemiologically relevant phthalate mixture and mono (2-ethyl-5-hydroxyhexyl) phthalate exposure alter cell energy metabolism in primary mouse granulosa cells,
Laws, M. J., Kramer, S., Gonyea, T., Huff, J., Edwards, L., Tarvainen, I., Damdimopoulou, P. and Flaws, J. A., *Reproductive Toxicology*, Aug 2025, Vol. 135.

Many products including plastic food containers, medical tubing, and personal care products contain phthalate diesters. Phthalates have been shown to negatively affect the female reproductive system. However, the ovarian cellular impacts of monoester phthalates, the metabolites of phthalate diesters, are largely unknown. This study tested the hypothesis that a monophthalate metabolite mixture or single monophthalate affects cell energy metabolism in granulosa cells. To test this hypothesis, granulosa cells were exposed to vehicle control, the mean urinary level and 100-fold higher monophthalate mixture (2.0 mu M and 200.0 mu M), or mono(2-ethyl-5hydroxyhexyl) phthalate (MEHHP) (0.22 mu M and 22.0 mu M) for 24 or 72 h. Gene expression was assessed for antioxidant enzymes, glycolytic enzymes, and glucose transporters. Cellular metabolism was assessed by Agilent Seahorse assays. MEHHP did not alter expression of the antioxidant enzymes, glycolytic enzymes, or glucose transporters compared to control. However, the monophthalate mixture significantly increased expression of Ldha (200.0 mu M, 72-hour exposure) and Glut1 (2.0 mu M, 24-hour exposure) compared to control. MEHHP (22.0 mu M) increased total ATP production rate at 24 h compared to control, but did not change total ATP production after 72 h. Further, the mixture (2.0 mu M and 200.0 mu M) altered total ATP production rates compared to control at the 72-hour and 24-hour time points. Short-term phthalate exposure led to significant effects on ATP production rates, making this endpoint a logical indicator of early phthalate toxicity. These data indicate that a monophthalate mixture as well as single monophthalate exposure alter cellular metabolism in granulosa cells.
https://doi.org/10.1016/j.reprotox.2025.108938

Impact of endocrine disrupting chemicals (EDCs) on epigenetic regulation in the uterus: a narrative review,
Liang, Y. J., Lu, Q. S., Chen, M. J., Zhao, X. M., Chu, C., Zhang, C. F., Yuan, J. H., Liu, H. M. and Lash, G. E., *Reproductive Biology and Endocrinology*, May 26 2025, Vol. 23, no. 1.

Endocrine disrupting chemicals (EDCs) are ubiquitous in the environment and have been shown to interfere with the endocrine system, leading to adverse effects on reproductive health. In females, EDC exposure has been linked to menstrual irregularities, infertility, and pregnancy complications. Epigenetic regulation, which involves modifications to DNA and histones that do not alter the underlying genetic code, plays a crucial role in female reproduction. EDCs have been shown to disrupt epigenetic mechanisms, leading to changes in gene expression that can have long-term effects on reproductive outcomes. Several EDCs, including bisphenol A (BPA) and phthalates, dioxins, and polychlorinated biphenyls (PCBs), have been shown to alter DNA methylation patterns and histone modifications in female reproductive tissues. These changes can lead to altered expression of genes involved in ovarian function, implantation, and placental development. Here, we integrate epidemiological and experimental evidence from the last 20 years to profile the types of diseases that EDCs trigger in the female reproductive system in relation to the uterus, and the corresponding molecular mechanisms that have been studied. In addition, this review will outline the state of knowledge of EDC epigenetic regulation in the uterus and how it impacts reproductive health, as well as identify areas for future research. https://doi.org/10.1186/s12958-025-01413-z

Novel insights into the causal relationship between endocrine-disrupting chemicals and breast cancer mediated by circulating metabolites,
Lin, Y. L., Zhang, Y., She, J., Zhao, R. D., Lin, S. J., Zhang, Y., Zhang, L. Y., Wei, J., Lin, Y. and Yang, Q. M., *Environmental Pollution*, Jun 15 2025, Vol. 375.

The relationship between endocrine-disrupting chemicals (EDCs) and breast cancer has not been extensively investigated. Although EDCs can disrupt human endocrine system, the underlying mechanism of EDCs on breast cancer requires further exploration. This study aimed to investigate the causal relationship between EDCs and breast cancer through Mendelian randomization (MR) and Generalised Summary-data-based Mendelian Randomization (GSMR) approach. Our results demonstrated that Bisphenol F was associated with increased risk of breast cancer [odds ratio (OR) = 1.018 (95 % CI 1.004-1.031), P = 0.010)]. Mono-(2-ethyl-5-carboxypentyl) phthalate (MECPP) was associated with lower breast cancer risk (OR = 0.894, 95 %CI = 0.819-0.975, P = 0.012). In addition, we identified 4 EDCs (bisphenol F, MECPP, Mono-ethyl phthalate, and Methyl paraben) significantly associated with ER + breast cancer. Furthermore, 3-bromo-5-chloro-2,6-dihydroxybenzoic acid mediated 10.9 % of the influence of MECPP on breast cancer. In addition, enrichment analysis was used to identify the pathways related to EDCs. MR-Phenome Wide Association Study (PheWAS) analysis was used to explore potential treatable diseases and adverse outcomes of EDCs. These findings shed light on the potential impact of EDCs exposure on breast cancer, which offer novel perspectives for future mechanistic and clinical research of EDCs and breast cancer.
https://doi.org/10.1016/j.envpol.2025.126349

Prostate cancer and pollution: Dangerous connections,
Magnifico, S., Hinault-Boyer, C., Bost, F. and Chevalier, N., *Annales D Endocrinologie*, Jun 2025, Vol. 86, no. 3.

Prostate cancer is the archetypal hormone-dependent cancer in men, mirroring breast cancer in women. The increase in its prevalence over time raises questions, and occupational exposure data, particularly among agricultural workers, have shown a probable or possible link with exposure to certain endocrine disruptors. The best-known of these is probably chlordecone, used in the French West Indies and responsible for an increased risk of prostate cancer. Outside these situations of occupational and/or acute exposure, it is more difficult to prove that endocrine disruptors are responsible for prostate cancer, particularly through epidemiological studies, the interpretation of which is still difficult. Animal models, in particular murine models, have demonstrated the role of fetal or early neonatal exposure in the development of prostate cancer in adulthood. In vitro models, meanwhile, are shedding light on the mechanisms involved in tumor promotion and progression, involving both classic hormone receptors (AR, ER) and other new signaling pathways. The aim of this review is to report the available data showing the link between exposure to endocrine disruptors and the risk of prostate cancer. (c) 2025 Elsevier Masson SAS. All rights are reserved, including those for text and data mining, AI training, and similar technologies.
https://doi.org/10.1016/j.ando.2025.101769

Glyphosate and AMPA-induced apoptosis and epigenetic alterations in HepG2 Cells: Upregulation of p53-BAX-CASP pathways,
Mehtiyev, T., Guler, Z. R., Aktan, E. and Ozden, S., *Food and Chemical Toxicology*, Sep 2025, Vol. 203.

Glyphosate and its metabolite aminomethylphosphonic acid (AMPA) are environmental contaminants with potential toxic effects. This study aimed to investigate apoptosis and epigenetic

alterations induced by glyphosate and AMPA in HepG2 cells. The IC50 values for glyphosate and AMPA were 6.19 mM and 8.13 mM, respectively, following 24 h exposure; mechanistic assays were conducted at sub-cytotoxic concentrations (50-500 mu M). Annexin V/PI flow cytometry revealed that AMPA significantly increased early apoptosis (up to 116 %, p < 0.001), while glyphosate elevated late apoptosis (up to 145 %, p < 0.001). Gene expression analysis showed significant upregulation of p53 (>= 1.49-fold), BAX (>= 1.82-fold), CASP3 (>= 1.37-fold), and CASP9 (>= 1.83-fold), with no significant change in BCL2. Epigenetic analysis indicated that both glyphosate and AMPA increased global DNA methylation, with fold changes ranging from 1.43 to 1.62-fold at concentrations of 100-250 mu M (p < 0.05). DNA methyltransferase genes DNMT1 (>= 2.44-fold), DNMT3A (>= 1.65-fold), and DNMT3B (>= 1.65-fold) were upregulated. Additionally, histone modification profiling showed elevated levels of H3K27me3, H3K9me3, and H3K9ac (p < 0.05), alongside increased expression of G9a (>= 1.64-fold), EZH2 (>= 2.14-fold), SETD1B (>= 2.15-fold), HAT1 (>= 2.40-fold), and SIRT1 (>= 2.57-fold), and downregulation of SUV39H1 (>= 0.27-fold). These findings reveal the molecular mechanisms of glyphosate and AMPA toxicity, linking apoptosis to epigenetic alterations and enhancing understanding of their risks.
https://doi.org/10.1016/j.fct.2025.115605

An in silico to in vivo approach identifies retinoid-X receptor activating tert-butylphenols used in food contact materials,
Mengeling, B. J., Ramaprasad, A. S. E., Smith, M. T., Turkieh, D., Kleinstreuer, N. C., Mansouri, K., Durkin, K. A., La Merrill, M. A. and Furlow, J. D., *Scientific Reports*, Jul 18 2025, Vol. 15, no. 1.

The potential for food contact chemicals to disrupt genetic programs in development and metabolism raises concerns. Nuclear receptors (NRs) control many of these programs, and the retinoid-X receptor (RXR) is a DNA-binding partner for one-third of the NRs. RXR disruption could generate adverse outcomes in several NR pathways. We used machine learning and other in silico methods to identify RXR-interacting candidates from a list of over 57,000 chemicals. Butylphenols comprised the largest, high-probability, structural group (58 compounds); several are food contact chemicals with widespread commercial use. In vitro ToxCast data suggested that bulky, aliphatic substitution at C4 of 2,6-di-tert-butylphenol facilitated RXR activation. We tested six butylphenols with increasing bulk at C4 in vivo for their ability to disrupt thyroid hormone receptor (TR) signaling, using an integrated luciferase reporter driven by TR-RXR binding and quantifiable morphological changes in a Xenopus laevis precocious metamorphosis assay. Three tert-butylphenols potentiated TH action at nanomolar concentrations. Molecular modeling showed the three positives formed more frequent, stable interactions with RXR alpha, and bulkiness at C4 increased steric complementarity with the RXR ligand-binding pocket. Our findings establish a paradigm for machine learning coupled with a convenient, in vivo validation approach to identify chemicals interacting with RXR-NR-controlled genetic pathways. https://doi.org/10.1038/s41598-025-09244-z

Dysregulation of microRNA (miRNA) Due to Phthalate/Phthalate Metabolite Exposure and Associated Health Effects: A Narrative Review,
Mohammed, A., Atkin, S. L. and Brennan, E., *Journal of Xenobiotics*, May 12 2025, Vol. 15, no. 3.

Phthalates, a group of synthetic non-persistent organic chemicals commonly used as solvents and plasticisers, have been associated with a range of detrimental health effects. These endocrine disrupting chemicals (ECDs) may exert their effects through epigenetic changes such as altered microRNA (miRNA) expression. miRNAs are short non-coding endogenous RNA transcripts that are preferentially expressed in various tissues and cell types and can circulate in body fluids, thereby regulating gene expression and acting as mediators for intercellular communication. As miRNAs mostly target protein-coding transcripts, they are involved in nearly all networks that regulate

developmental and pathological processes. In this review, we provide an overview of human, in vivo and in vitro studies assessing altered miRNA expression due to phthalate exposure and their biological effects. Importantly, this study suggests that the mechanism of phthalate action may in part be mediated by epigenetic changes, affecting a large number of different proteins. This is indicative that alterations in miRNA expression induced by phthalate exposure are then implicated in a wide range of health conditions, including reproductive dysfunction, oncogenesis, metabolic disorders, and neurodevelopmental outcomes. Exposure to phthalates and their metabolites predominantly results in the upregulation of miRNAs. Dysregulation of miR-34a, miR-15b, miR-141, miR-184, miR-19a, miR-125, and miR-let-7 were observed across several studies. More research involving human participants combined with mechanistic studies integrating mRNA target analysis would be beneficial in understanding the downstream effects of phthalate exposure on gene expression and grasping the broader biological implications. https://doi.org/10.3390/jox15030072

Unraveling the Core of Endometriosis: The Impact of Endocrine Disruptors,
Moustakli, E., Potiris, A., Grigoriadis, T., Zikopoulos, A., Drakaki, E., Zouganeli, I., Theofanakis, C., Gerede, A., Zachariou, A., Domali, E., Drakakis, P. and Stavros, S., *Int J Mol Sci*, Aug 6 2025, Vol. 26, no. 15.

Globally, endometriosis affects almost 10% of reproductive-aged women, leading to chronic pain and discomfort. Endocrine-disrupting compounds (EDCs) seem to play a pivotal role as a causal factor. The current manuscript aims to explain potential molecular pathways, synthesize current evidence regarding EDCs as causative agents of endometriosis, and highlight implications in the general population and clinical work. A thorough review of experimental, epidemiologic, and mechanistic research studies was conducted to explain the association between EDCs and endometriosis. Among the primary EDCs under investigation are polychlorinated biphenyls, dioxins, phthalates, and bisphenol A (BPA). Despite methodological heterogeneity and some discrepancies, epidemiologic evidence supports a positive association between some increased levels of BPA, phthalates, and dioxins in urine or in blood, and endometriosis. Experiments support some effect of EDCs on endometrial cells and causing endometriosis. EDCs function as xenoestrogens, alter immune function, induce oxidative stress, and disrupt progesterone signaling. Epigenetic reprogramming may play a role in mediating EDC-induced endometriosis. Endocrine, immunological, and epigenetic pathways link EDCs and endometriosis. Prevention techniques require deeper comprehension of those factors. Causal linkages and possible treatment targets should be based on longitudinal studies and multi-omics techniques. Restriction of EDCs could be beneficial for endometriosis prevalence limitation. https://doi.org/10.3390/ijms26157600

Effects of Bisphenol A and Retinoic Acid Exposure on Neuron and Brain Formation: A Study in Human Induced Pluripotent Stem Cells and Zebrafish Embryos,
Nishie, T., Taya, T., Omori, S., Ueno, K., Okamoto, Y., Higaki, S., Oka, M., Mitsuishi, Y., Tanaka, T., Nakamoto, M., Kawahara, H., Teraguchi, N., Kotaka, T., Sawabe, M., Takahashi, M., Kitaike, S., Wada, M., Iida, K., Yamashita, A., Jinno, H., Ichimura, A., Tooyama, I., Sakai, N., Hibi, M., Hirasawa, A. and Takada, T., *Environmental Health Perspectives*, Jun 2025, Vol. 133, no. 6.

BACKGROUND: Developing human fetuses may be exposed to the chemical compound bisphenol A (BPA), and retinoic acid (RA) has been detected at low levels in water sources. RA signaling regulates key developmental genes and is essential for organ development, including the brain. We previously reported that RA/BPA coexposure of mouse embryonic stem cells potentiates RA signaling, which warrants further investigation. OBJECTIVE: This study was undertaken in human induced pluripotent stem cells (iPSCs) and zebrafish embryos to investigate whether coexposure to BPA and exogenous RA could potentiate HOX gene expression and exert pleiotropic effects on RA

signaling. METHODS: Human iPSCs and zebrafish embryos were exposed to exogenous RA (0, 7.5, 10, 12.5, 100, 200 or 500 nM) or BPA (20 lM) alone or coexposed to BPA (2 nM-20 lM) and exogenous RA (7:5-100 nM). Postexposure changes in HOX genes were assessed by quantitative polymerase chain reaction and/or transcriptome analyses. RA receptor antagonists were used to identify the receptor responsible for signaling. In zebrafish, spatial expression of fgf8a and hoxb1a was evaluated by whole-mount in situ hybridization. Mauthner cell and craniofacial cartilage anomalies were studied by immunostaining and Alcian blue staining, respectively. Transcriptome was compared between iPSCs and zebrafish to identify alterations of common biological processes. Gradient curves of RA signal were calculated to simulate the effects of exogenous RA and BPA in zebrafish. RESULTS: In both iPSCs and zebrafish, RA/BPA coexposure had higher expression of 30 HOX genes in comparison with RA alone; BPA alone had no effect. Addition of RA receptor antagonists abolished these changes. In zebrafish, RA/BPA coexposure, in comparison with RA alone, resulted in a significant rostral shift in hoxb1a expression and increased rate of anomalies in Mauthner cells and craniofacial cartilage. Transcriptome comparison and correlations between the experimental results and gradient curve simulations strengthened these observations. CONCLUSION: Our findings suggest a mechanistic link between chemical exposure and neurodevelopmental impairments and demonstrate involvement of exogenous RA signaling in endocrine disruption. Further investigation is needed to explore why BPA alone did not affect endogenous RA signaling, whereas exogenous RA signaling was potentiated with RA/BPA coexposure. https://doi.org/10.1289/EHP15574 https://doi.org/10.1289/ehp15574

Implications of plastic-derived endocrine disruptors on human health,
Ojo, A. B., Agbeye, O. D., Ogwa, T. O., Adedoyin, D., Rotimi, D. E. and Ojo, O. A., *Toxicology Mechanisms and Methods*, 2025.

Endocrine-disrupting chemicals (EDCs), such as bisphenol A (BPA), bisphenol S (BPS), phthalates, and micro- and nanoplastics, present substantial environmental and health hazards because of their potential to disrupt hormonal systems. Micro- and nanoplastics can release EDCs that disrupt reproductive and developmental processes, potentially affecting future generations. BPA, a common plasticizer and resin component, mimics estrogen and disrupts thyroid hormone metabolism, contributing to obesity, diabetes, and cardiovascular issues. BPS, a BPA substitute, exhibits similar endocrine-disrupting properties and persists longer in the environment. Phthalates, which are widely used as plasticizers, are associated with reproductive issues, metabolic conditions, and developmental issues in children. Combined exposure to multiple EDCs can amplify health risks, underscoring the need for further research on the synergistic impacts of these chemicals. This review underscores the urgent need for effective regulatory measures and further investigations into the health impacts of EDCs to mitigate their harmful impacts on the health of humans and the environment. https://doi.org/10.1080/15376516.2025.2510525

Environmental endocrine disruptors: rethinking the origins of early-onset ER(+) breast cancer,
Parrish, M. and Kuperwasser, C., *Nat Rev Cancer*, Jul 22 2025.
https://doi.org/10.1038/s41568-025-00854-3

Bisphenol A and reproductive health: a comprehensive overview of toxicological effect,
Reyaz, A., Javaid, D., Qadri, S. S., Ganie, S. Y. and Reshi, M. S., *Toxicological Research*, 2025.

Bisphenol A (BPA), a synthetic compound extensively used in the production of polycarbonate plastics and epoxy resins, is a pervasive environmental contaminant and a potent endocrine disruptor. By mimicking oestrogen and binding to oestrogen receptors, BPA interferes with normal hormonal signalling, leading to significant disruptions in reproductive systems. In males, BPA

exposure has been linked to reduced sperm count, impaired spermatogenesis, and histopathological alterations in testicular tissue, including disrupted Leydig cell function. In females, it affects ovarian follicle development, disrupts reproductive cyclicity, and causes morphological abnormalities in ovarian tissues. These reproductive effects are exacerbated by BPA-induced oxidative stress, which damages cellular structures and exacerbates hormonal imbalances. The mechanisms underlying BPA's reproductive toxicity involve disruptions in gene expression, signalling pathways, and hormonal homeostasis, highlighting its far-reaching effects on both male and female fertility. This study explores the hormonal havoc caused by BPA exposure, emphasizing its multifaceted impact on reproductive health and the urgent need for mitigative strategies to address its toxicity. https://doi.org/10.1007/s43188-025-00305-z

Zearalenone and its metabolites provoke contrasting modulatory responses on estrogen and androgen receptors: Insights into the molecular basis of endocrine disruption in live cells, Rizvi, S., Chhabra, A., Sagurthi, S. R. and Tyagi, R. K., *Food and Chemical Toxicology*, Sep 2025, Vol. 203, p. 16.

Zearalenone (ZEA) is a non-steroidal mycotoxin enrouted mainly through the consumption of contaminated dietary products. Some traditional studies with ZEA have implied influence on several cellular and endocrine processes. However, detailed advanced insights into the molecular basis of ZEA-induced toxicity under defined live-cell conditions remain unexplored. This study uses molecular docking and cell-based approaches to investigate the interactions between ZEA, its metabolites (a-ZOL, (3-ZOL), steroid receptors ERa/(3, and androgen receptor (AR). The studies were performed with HEK293T and HepG2-derived stable cell lines exposed to 1 mu M of ZEA, a-ZOL, (3-ZOL, and cognate steroids, 17(3-estradiol, and 5a-DHT (10 nM). Fluorescent protein-tagged cytoplasmic-shifted ERa/(3 and AR chimeras enabled visualization of receptor-xenobiotic interactions under live-cell conditions. Key parameters examined included i) receptor subcellular localization, ii) ligand-receptor interactions, iii) transcriptional function, and iv) receptor-chromatin interactions. Competitive reporter-gene assays were also performed with a-ZOL and (3-ZOL (0.1-1.0 mu M) in the presence of 5a-DHT (EC50; 10-10 M). ZEA metabolites promoted i) ERa/(3 and AR nuclear translocation, ii) ERa/(3 transactivation, iii) repression of DHT-induced AR transactivation, and iv) contrasting receptor-chromatin interactions. This study suggests that endocrine disruptions are driven by a complex interplay of agonistic and/or antagonistic effects of ZEA and its metabolites on receptor function, contributing to potential health risks. https://doi.org/10.1016/j.fct.2025.115593

Differential susceptibility of Leydig and Sertoli cells to bisphenol A, Ryu, D., Pang, W. K., Rahman, M. S., Park, Y. J. and Pang, M. G., *Toxicology*, Sep 2025, Vol. 516.

Bisphenol A (BPA) is an endocrine-disrupting chemical that is increasingly becoming a vital factor in public health due to its ubiquity and toxicity. BPA is associated with male infertility via the disrupted function of Leydig and Sertoli cells. Despite extensive research, the current understanding of the specific pathological concentrations and the mechanisms following BPA exposure still remain questionable. Therefore, we investigated the susceptibilities and underlying mechanisms in Leydig and Sertoli cells following treatment with various BPA doses (0.0001-100 mu M in a 10-fold serial dilution). Our results showed that the lowest BPA levels (10-4 mu M) decreased mitochondrial membrane potential and ATP levels. In contrast, ROS levels were increased at high BPA levels regardless of exposure time (24 or 48 h) in both cell types. Mitochondrial-mediated apoptosis was identified along with increased ROS levels and abnormal mitochondrial dynamics, but both cell types showed different susceptibility to BPA toxicity. Subsequently, BPA had detrimental impacts on the mRNA expression levels of steroidogenic enzymes and testosterone synthesis in Leydig cells and reduced anchoring junction proteins in Sertoli cells. Consequently, our results demonstrated that

both cells were affected via estrogen receptor alpha. However, protein kinase A was oppositely expressed following BPA exposure in each cell type. Therefore, it is plausible to suggest that each cell has distinct sensitivities and mechanisms in response to BPA.
https://doi.org/10.1016/j.tox.2025.154182

Potential effects of environmental toxicants on sperm quality and potential risk for fertility in humans,
Sciorio, R., Greco, P. F., Greco, E., Tramontano, L., Elshaer, F. M. and Fleming, S., *Frontiers in Endocrinology*, May 21 2025, Vol. 16.

Semen quality is a key factor in male fertility, but defining normal reference values for semen parameters remain challenging. Over the past four decades, several authors have reported a noticeable decline in sperm parameters, raising concerns about male reproductive health. While the exact causes remain unclear, potential contributors include environmental pollution, endocrine disruptor chemicals (EDCs) and oxidative stress, with the latter becoming a growing concern. Environmental changes and increased exposure to EDCs, such as pesticides, herbicides, bisphenol A (BPA), phthalates, polychlorinated biphenyls (PCBs), and heavy metals, are believed to contribute significantly to the decline in sperm quality. These chemicals impact individuals from prenatal life through adulthood, potentially leading to long-term reproductive consequences. Overall, this review explores the relationship between environmental toxicants, including volatile organic compounds, EDCs, as well as oxidative stress and reduced male fertility. While a substantial body of research has found associations between these exposures and adverse fertility outcomes, some studies have reported no significant associations. The primary objective of this review is to provide a deeper understanding of the potential mechanisms between these environmental chemicals on testicular function and spermatogenesis. It also examines the broader evidence on the decline in sperm quality and explores its potential implications for overall fertility outcomes in humans. By doing so, the review will shed light on the broader public health implications of environmental pollutants and their impact on male reproductive health, emphasizing the need for further research in this critical area. https://doi.org/10.3389/fendo.2025.1545593

Estrogenic and transgenerational effects of perfluorocarboxylic acids through estrogen-related receptor γ pathway,
Shi, S., Zheng, W., Zhang, X. L., Li, M. J., Ye, C., Chen, L., Hong, W. J., Li, C. H., Chi, H. Y., Li, F. F. and Guo, L. H., *Journal of Hazardous Materials*, Sep 5 2025, Vol. 495.

The estrogen-disrupting effects and mechanism of perfluorocarboxylic acids (PFCAs), with similar structures to perfluorooctanoic acid (PFOA), are poorly understood. The purpose of the present study is to explore the estrogen-disrupting effects of PFCAs through the estrogen-related receptor gamma (ERR gamma) pathway. In vitro, similar to an ERR gamma agonist, perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), PFOA, perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA) induced proliferation of human endometrial cancer cell Ishikawa at human exposure-related concentrations by binding and activating ERR gamma. In vivo, PFHxA, PFOA and PFDA induced ovarian damage in zebrafish at 3.2 mu M, 2.4 mu M and 1.9 mu M, respectively. PFCAs also induced sex hormones disturbance and interfered with sex hormone synthesis- and ERR gamma pathway-related gene expression. In particular, PFOA exhibited estrogen-disturbing effects at the environmentally relevant concentration. Maternal exposure to PFCAs produced abnormal development of zebrafish offspring by disturbing the sex hormones and ERR gamma pathway-related gene expression. All the effects were mitigated by an ERR gamma antagonist. In conclusion,PFCAs could cause estrogen-disrupting effects and transgenerational

effects through the ERR gamma pathway. The study revealed a novel insight into the estrogen-disrupting effects of PFCAs. https://doi.org/10.1016/j.jhazmat.2025.138994

Interference with systemic negative feedback as a potential mechanism for nonmonotonic dose-responses of endocrine-disrupting chemicals,
Shi, Z. Z., Xiao, S. and Zhang, Q., *Toxicological Sciences*, Aug 2025, Vol. 206, no. 2.

Environmental endocrine-disrupting chemicals (EDCs) often exhibit nonmonotonic dose-response (NMDR) relationships, posing significant challenges to health risk assessment and regulations. Several molecular mechanisms operating locally in cells have been proposed; however, whether and how systemic negative feedback-a global structure of all homeostatic endocrine systems-may render NMDRs is poorly understood. We hypothesized that an EDC may produce nonmonotonic effects by competing with the endogenous hormone for receptors simultaneously (i) at the central site to interfere with the feedback regulation and (ii) at the peripheral site to disrupt the hormone's endocrine action. We constructed a dynamical model of a generic hypothalamic-pituitary-endocrine axis with negative feedback to evaluate the hypothesis and biological conditions that favor NMDR. Our modeling found that when an EDC interferes sufficiently with the central feedback action, the net endocrine effect at the peripheral target site can be opposite to what is expected of an agonist or antagonist at low concentrations. J/U or Bell-shaped NMDRs arise when the EDC has differential binding affinities and/or efficacies, relative to the endogenous hormone, for the peripheral and central receptors. Novel quantitative relationships between these biological parameter variabilities and associated distributions were discovered, which can distinguish J/U and Bell-shaped NMDRs from monotonic responses. In conclusion, the ubiquitous negative feedback regulation in endocrine systems may act as a universal mechanism for counterintuitive and nonmonotonic effects of EDCs. Depending on the key receptor kinetic and signaling properties of EDCs and endogenous hormones, certain individuals may be more susceptible to these complex endocrine effects.
https://doi.org/10.1093/toxsci/kfaf060

Exploring the toxicological network in diabetic microvascular disease,
Song, S. Y., Huang, L. J., Zhou, X. Q. and Yu, J. Y., *International Journal of Surgery*, Jun 2025, Vol. 111, no. 6, p. 3895-3907.

Purpose:This study investigates how endocrine-disrupting chemicals contribute to diabetic microvascular disease.Methods:This study assessed endocrine-disrupting chemical toxicity using PubChem, ProTox 3.0, and ChEMBL. Relevant EDC targets were identified via SwissTargetPrediction and Similarity Ensemble Approach. Gene targets for diabetic microvascular diseases (diabetic kidney disease, retinopathy, and sensory polyneuropathy) were retrieved from CTD, GeneCards, and OMIM. Candidate targets were identified by intersecting EDC and disease-related targets. A protein-protein interaction network was built using STRING to identify hub genes. Functional enrichment analysis was conducted via Metascape. Molecular docking of EDC compounds with hub targets was performed using Discovery Studio and CDOCKER. Hub targets were validated through immunohistochemical staining, single-cell distribution, subcellular localization assays, and gene expression analysis in external HPA and GEO datasets.Results:A total of 843, 474, and 623 potential toxic targets were identified for diabetic kidney disease, diabetic retinopathy, and diabetic sensory polyneuropathy, respectively. KEGG pathway analysis linked EDC toxicity in diabetic kidney disease to key pathways such as cancer, chemokine signaling, apoptosis, calcium signaling, and drug metabolism (cytochrome P450), with hub targets including EGFR, ALB, MYC, ESR1, and HSP90AA1. Diabetic retinopathy was associated with MAPK, ERBB, NOD-like receptor signaling, and renal cell carcinoma pathways, with ALB, EGFR, MYC, BCL2, and CD4 identified as hub targets. For diabetic sensory polyneuropathy, EDCs may influence chemokine, apoptosis, ERBB, VEGF, and JAK-STAT

signaling pathways, with ALB, EGFR, MYC, ESR1, and BCL2 as key targets. Molecular docking confirmed strong binding activity between EDC components and hub targets.Conclusion:This study offers a theoretical basis for identifying toxic targets and mechanisms by which endocrine-disrupting chemicals contribute to diabetic microvascular diseases.
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Burden of per- and polyfluoroalkyl substances (PFAS) in human breast milk: Implications for maternal and infant health,
Su, J. H., Gao, Y. R., Sun, Y. M., Bing, M. Y., Liu, Q. S., Zhou, Q. F., Fiedler, H. and Jiang, G. B., *Environment International*, Jul 2025, Vol. 201.

Per-and polyfluoroalkyl substances (PFAS) are frequently detected in human breast milk. However, there is still limited understanding of the potential health risks associated with PFAS contamination in breast milk. In the present study, we calculated the plasma concentrations and estimated daily intakes (EDIs) of four PFAS, i.e. perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS) and perfluorononanoic acid (PFNA), based on a recently published study on PFAS concentrations in breast milk from five regions of the United Nations, and evaluated the potential health risks of PFAS. Risk assessment based on plasma PFAS concentrations indicated their potential deleterious effects on both mothers and infants, and notably infants were more vulnerable than mothers to PFAS exposure. Moreover, PFHxS and PFNA posed a higher health risk than PFOS and PFOA. Based on the calculation of toxicological data from animal studies using the method proposed by the Agency for Toxic Substances and Disease Registry (ATSDR), new minimal risk values (MRVs) proposed herein for infants were 3.35, 2.92, 0.25, and 0.38 ng/kg bw/d for PFOS, PFOA, PFHxS, and PFNA, respectively. The comparison of infant MRVs and EDIs further demonstrated the health hazards of PFAS exposure in infants via breast milk. This work indicated the potential maternal and infant health risks from human burden of PFAS, and the newly developed MRVs of four PFAS for infants would be more suitable than the health-based guidance values proposed by the ATSDR, in view of accurate assessment on the health threat to neonates from the exposure of this kind of emerging chemicals via breastfeeding.
https://doi.org/10.1016/j.envint.2025.109593

Molecular insights into the interaction mechanism of endocrine-disrupting chemicals and DNA in laccase-induced polymerization transfer,
Sun, K., Shi, Z. Y., Dai, L. Z., Si, Y. B., Ma, J. C., Lin, H. and Yu, H. Q., *Pnas Nexus*, May 2025, Vol. 4, no. 5.

Endocrine-disrupting chemicals (EDCs), such as 17 beta-estradiol (E2) and bisphenol A (BPA), can induce DNA damage, leading to genomic instability and cell death. Laccase, an enzyme secreted by diverse organisms, plays a critical role in mitigating the cytotoxicity of these contaminants. Despite its importance, the dynamic evolution and interaction mechanisms of EDCs and DNA in laccase catalysis remain poorly understood. This study investigates the interactions between EDCs and DNA during laccase-induced polymerization transfer at a molecular level. As the DNA concentration was increased from 0 to 7.575 nM, the pseudo-first-order kinetic constants for E2 and BPA decreased by 2.03 and 2.10 times, respectively. DNA-bound EDCs disrupted the catalytic activity and stability of laccase, thereby delaying the polymerization transfer rate of EDCs. E2 and BPA bound to DNA base pairs via groove and intercalative modes, respectively. Laccase-induced polymerization reduced damage to the DNA helix and base stacking caused by EDC binding. Moreover, the resulting DNA-EDC-precipitated polymers, formed through continuous laccase polymerization, exhibited denser and more complex structures compared with spherical EDC-precipitated polymers, confirming DNA encapsulation and/or binding. This work underscores the intramolecular mechanisms of EDC

interaction with DNA in vitro during the laccase-induced polymerization, offering efficient ways to mitigate the genotoxicity of EDCs. https://doi.org/10.1093/pnasnexus/pgaf148

Bisphenol A Promotes the Progression of Hormone-Sensitive Breast Cancers Through Several Inflammatory Pathways,
Thoene, M., Zglejc-Waszak, K., Jozwik, M. and Wojtkiewicz, J., *Cancers (Basel)*, Jul 17 2025, Vol. 17, no. 14.

Background/Objectives: Bisphenol A (BPA) is found throughout the environment and exposure to it has been shown to cause several health problems, including cancer. The problem with BPA is that it is a xenoestrogen that is chemically very similar to 17β-estradiol. Chronic exposure to BPA overstimulates the estrogen receptors and leads to inflammation that triggers several pathways leading to cancer progression. This is especially true in the case of hormone-sensitive breast cancers. This article reviewed the main pathways thought to be involved in the formation and/or progression of the most common forms of hormone-sensitive breast cancers due to BPA exposure. The main results were compiled and presented in tables along with a more detailed discussion of each pathway within the text. In most cases, chronic BPA exposure led to inflammation, which then triggered pathways leading to cancer stem cell formation and maintenance. In other cases, BPA exposure led to the formation of reactive oxygen species that damaged DNA and caused the formation of mutated p53 and tumorigenesis. Conclusions: The article summarizes the key pathways that are currently known, pertaining to how BPA leads to the progression and maintenance of breast cancer. The article then concludes by discussing how prenatal and perinatal BPA exposure may also predispose women to hormone-sensitive breast cancers later in life.
https://doi.org/10.3390/cancers17142373

Release of Bisphenol A from Dental Materials: Risks and Future Perspectives,
Tichy, A., Srolerova, T. and Schwendicke, F., *Journal of Dental Research*, Sep 2025, Vol. 104, no. 10, p. 1051-1060.

The gradual phaseout of dental amalgam has contributed to a significant increase in the use of resin-based materials. While these materials offer several desirable properties, concerns persist regarding their biocompatibility, particularly the release of bisphenol A (BPA). BPA is an endocrine-disrupting chemical linked to adverse effects on human health, including reproductive, developmental, and metabolic disorders. Although food contact materials are the primary source of human BPA exposure and the contribution of dental materials is minor, the associated risks cannot be dismissed due to BPA's nonmonotonic dose-response relationship. In 2023, the European Food Safety Authority proposed a 20,000-fold reduction in the tolerable daily intake of BPA to 0.2 ng/kg body weight, citing immune system effects at extremely low doses. This proposal has sparked regulatory and scientific debate, as adopting such a stringent limit would effectively ban the use of BPA in food contact materials and many other products. Given this context, it is essential to assess the release of BPA from dental materials both in vitro and in vivo. However, data interpretation is complicated by methodological inconsistencies, including variations in material composition, specimen preparation, choice of extraction media, experimental duration, and analytical methods. In addition, pivotal differences in reporting results make it difficult to synthesize findings and draw reliable conclusions. This review examines the controversy surrounding BPA, critically evaluates evidence on its release from dental materials, and explores mitigation strategies. By highlighting gaps in knowledge and proposing future research directions, this review aims to provide clinicians, researchers, and policymakers with a clearer understanding of BPA-related complexities, ultimately contributing to patient safety and material innovation.
https://doi.org/10.1177/00220345251337728

The impact of bisphenol A and its analogs on female reproductive health,
Trela-Kobedza, E. and Ajduk, A., *Reproductive Biology*, Sep 2025, Vol. 25, no. 3.

The number of pollutants stemming from anthropogenic chemicals is increasing every year. Some of them act similarly to hormones and are referred to as endocrine-disrupting chemicals or endocrine disruptors. In this group, bisphenol A (BPA) is well characterized as a xenoestrogen and is known to affect human health. BPA is crucial to the production of plastic, a material that has revolutionized and facilitated daily life. Nevertheless, the use of BPA is currently being limited, and consequently, new BPA analogs are under development. However, both BPA and its analogs can be released into the environment during their manufacturing process and daily usage. In conjunction with the escalating demand for plastics and the prolonged persistence of plastic waste, it poses a substantial threat to human health. In this article, we concentrate on the influence of BPA and its most common analogs (bisphenol S, bisphenol F, bisphenol AF, bisphenol Z, bisphenol P, bisphenol AP, bisphenol B) on female reproductive health. We reviewed the existing epidemiological data (or in the absence of it, data obtained from animal and in vitro models) on their impact on hormone levels, oocyte yield, oocyte and embryo quality, implantation and pregnancy success, polycystic ovary syndrome, and endometriosis. We also discuss metabolism of bisphenols, their mechanism of action and impact on cellular physiology, as well as current regulations on their use. Our comprehensive review reveals that, despite existing discrepancies, a substantial body of evidence suggests that bisphenols influence female reproductive health. This underscores the urgent need for future regulatory measures to limit and regulate the use of bisphenols. https://doi.org/10.1016/j.repbio.2025.101028

Micro- and Nanoplastics as Disruptors of the Endocrine System-A Review of the Threats and Consequences Associated with Plastic Exposure,
Tyc, H. J., Klodnicka, K., Teresinska, B., Karpinski, R., Flieger, J. and Baj, J., *International Journal of Molecular Sciences*, Jun 26 2025, Vol. 26, no. 13.

Plastic overconsumption has emerged as a major environmental pollutant, with degraded micro- and nanoplastic (MNP) particles being consumed by a vast variety of species. MNPs, particles < 5 mm, contain endocrine-disrupting chemicals (EDCs), which can bind to hormone receptors and disrupt the proper endocrinological function of a variety of organs. This review explores the toxicological impact of MNPs on the hypothalamus, pituitary gland, thyroid, pineal body, ovaries, and testes, as well as the effects of the endocrinological regulatory axes, including the hypothalamic-pituitary-gonadal (HPG), hypothalamic-pituitary-thyroid (HPT), and hypothalamic-pituitary-adrenal (HPA) axes. The disruption of these hormonal feedback systems leads to reproductive dysfunction, neurotoxicity, cytotoxicity, immunotoxicity, and metabolic disorders. The gonads are particularly susceptible, with studies demonstrating oxidative stress, cellular apoptosis, and infertility due to MNP exposure. Given the widespread presence of MNPs and their impact on human health, further research is critical to understand their long-term effects and develop strategies to reduce exposure. https://doi.org/10.3390/ijms26136156

The sources, distribution and toxicological effects on humans of polyhalogenated carbazoles (PHCZs) as a novel pollutant,
Wang, X. X., Zhang, D. J., Liu, S. Y., Xin, H., Guan, J. L., Zhang, Y. F. and Zhang, R., *Ecotoxicol Environ Saf*, Aug 1 2025, Vol. 303, p. 118793.

Polyhalogenated carbazoles (PHCZs) are a new type of organic pollutants, characterized by its environmental persistence, bioaccumulation property, and toxicity similar to dioxins. The pervasive environmental presence of PHCZs, coupled with their heterogeneous spatial distribution, has

garnered increasing scientific attention. Furthermore, studies have detected PHCZs in humans and demonstrated their toxic effects. Therefore, this study aims to conduct a more in-depth investigation and analysis of the systemic toxicity of PHCZs in humans and their specific molecular mechanisms. This review delves into the toxicological effects of PHCZs on humans, categorizing them into cardiotoxicity, neurotoxicity, hepatotoxicity and endocrine disruption. It also explores their metabolic transformation in the human body, ecotoxicological effects and potential degradation strategies. The content covers analytical methods, environmental occurrence patterns, ecological impacts, degradation mechanisms and prevention and control measures. This work clarifies the specific toxicological effects of PHCZs on humans, provides new therapeutic directions for future disease treatment, and enhances the environmental risk assessment and management of PHCZs. https://doi.org/10.1016/j.ecoenv.2025.118793

Exploring thyroid development and function: A systems biology search for new chemical disruptor targets,
Zenzeluk, J., Oliveira, J. M., Sater, A. C., Bargi-Souza, P., Romano, M. A., Serrano-Nascimento, C. and Romano, R. M., *Molecular and Cellular Endocrinology*, Sep 15 2025, Vol. 607.

Indiscriminate exposure to chemical substances has emerged as a critical global health concern. Human exposure to emerging contaminants, including pharmaceutical residues, pesticides, food additives, and chemicals employed in packaging and bottle production, is associated with an increased incidence of diseases, including thyroid disorders. Several chemicals potentially dysregulate thyroid embryonic development and the adult hypothalamic-pituitary-thyroid (HPT) axis. In this study, we applied systems biology approaches to identify biological processes associated with the most highly upregulated and downregulated genes in human thyroid transcriptome data from both the embryonic and adult stages. As a result, new gene/protein-chemical interactions linked to recognized toxicities in the thyroid gland and the HPT axis were identified. This analysis identified 195 distinct chemical substances that may interact with these highly expressed proteins and exhibit thyroid toxicity. Our findings underscore the developmental period as a critical window of vulnerability to chemical exposure, with potential adverse effects on thyroid development and programming. Finally, our data suggest new targets for emerging chemicals in the thyroids of adult individuals, potentially compromising thyroid function. https://doi.org/10.1016/j.mce.2025.112609

Mechanisms and rescue measures of female ovarian dysfunction induced by environmental endocrine chemicals: A review,
Zhang, J. L., Zhang, N., Mai, Q. Y. and Zhou, C. Q., *Reproductive Toxicology*, Aug 2025, Vol. 135.

Environmental endocrine chemicals (EDCs) constitute a class of exogenous chemicals with the capacity to imitate or impede the processes of synthesis, secretion, transport, conjugation, reaction, and metabolism of natural hormones in living organisms. They elicit a broad spectrum of physiological effects, which may either mirror those of natural hormones or exhibit anti-natural characteristics. Prolonged exposure to EDCs has been demonstrated to exert significant effects on animal reproduction and development. It is noteworthy that the female reproductive system is more susceptible to the effects of EDCs than the male reproductive system. EDCs have the potential to cause significant damage to the structure and function of the female reproductive organs, and have been linked to an increased incidence of various tumors in the female reproductive system, including ovarian cancer. A growing body of evidence suggests that exposure to EDCs affects reproduction in five main ways: competitively binding to cell membrane-specific receptors, disruption of cellular signaling within germ cells, intracellular imbalance between reactive oxygen species and antioxidants, alteration of epigenetic modifications, and control of early apoptosis. Nevertheless, the same in vivo and in vitro studies have indicated that the reproductive toxicity produced by EDCs

can also be attenuated in a multitude of ways, such as by antioxidants, hormones, and compensatory mechanisms of signal transduction. Through comprehensive analysis of epidemiological studies, laboratory experiments, and clinical observations, this review details the mechanisms of the effects of EDCs leading to ovarian dysfunction and proposes a series of strategies to prevent EDCs exposure. https://doi.org/10.1016/j.reprotox.2025.108954

Impact of endocrine disrupting chemicals on macrophages at the maternal-fetal interface, Zhao, B., Lu, Q. S., Chen, M. J. and Lash, G. E., *Seminars in Immunopathology*, Jul 16 2025, Vol. 47, no. 1.

Pregnancy is a complex and dynamic process, immune homeostasis at the maternal-fetal interface is one of the keys to a successful pregnancy and essential for fetal nutrient exchange and the establishment of immune tolerance. Healthy pregnant women with normally functioning immune systems can successfully maintain a semi-allogeneic fetus to full term without immune-mediated rejection, many immune cells including macrophages, NK cells, T cells, B cells and dendritic cells are involved in this process. In particular, macrophages play a vital role in the establishment of immune tolerance, infection prevention, spiral artery remodeling, and overall maternal and fetal health, due to their plasticity and diversity. However, environmental toxins like endocrine-disrupting chemicals (EDCs) can impact macrophage function, leading to pregnancy-related conditions. This review explores the current knowledge of macrophages at the maternal-fetal interface, their roles in pregnancy, and how EDCs affect their polarization and function. https://doi.org/10.1007/s00281-025-01055-8

Evaluation de l'exposition

Persistent organic pollutants in human milk of Belgian mothers: levels, time trend and exposure assessment for nursing infants, Andjelkovic, M., Van Overmeire, I., Joly, L., Poma, G., Malarvannan, G., Vleminckx, C., Malysheva, S. V., Vanhouche, M., Van Loco, J., Van Nieuwenhuyse, A. and Covaci, A., *Journal of Environmental Exposure Assessment*, Dec 2024, Vol. 3, no. 4.

Human milk samples (n = 206) collected in 2014 from Belgian primiparous mothers were analyzed for seven groups of persistent organic pollutants (POPs): dichlorodiphenyltrichloroethane and its metabolites (DDTs), chlordane compounds (CHLs), hexachlorocyclohexane isomers (HCHs), hexachlorobenzene (HCB), polybrominated diphenyl ethers (PBDEs), pentachlorobenzene (PeCB), and hexabromobiphenyl (BB-153). Pooled samples for the analysis of hexachlorobutadiene, heptachlor, chlordecone, dieldrin, and hexabromocyclododecane (HBCD) were prepared. DDTs [median: 41 ng/g lipid weight (lw)], HCB (5.5 ng/g lw), and HCHs (2.4 ng/g lw) were the predominant compounds in all samples. Median levels of PBDEs (0.91 ng/g lw) in Belgian human breast milk samples were lower compared to other European countries. The major PBDE congeners were BDE-47 and BDE-153, and total PBDE levels were low (0.30-4.25 ng/g lw). alpha-HBCD was the only HBCD stereoisomer found in the pooled milk samples (2.5 ng/g lw). All targeted POPs were determined in a national pooled sample but were lower than levels of most POPs [organochlorine pesticides (OCPs), PBDEs, and polychlorinated biphenyls (PCBs)] observed in 2006. The daily dietary intake of POPs via human milk was estimated for nursing infants of 1 month [intake of 260 mL milk/kg body weight (bw)] and compared with either health-based guidance values (HBGV) or the reference point (margin of exposure, MOE). The exposure assessment in a worst-case scenario revealed no concern for most POPs. However, the infants were exposed to levels of 60 pg total WHO2005-TEQ/kg bw/week, indicating a possible risk during their life. Based on the MOE approach,

95th percentile of concentration can result in a health concern for congeners BDE-99 and BDE-153. https://doi.org/10.20517/jeea.2024.22

Bio-monitoring of endocrine disrupting chemicals in human serum: insights from a study in Central India,
Sharma, P., Pal, N., Singh, S., Ojha, R., Kumawat, M., Shubham, S., Verma, V., Tiwari, R. R., Sarma, D. K. and Kumar, M., *International Journal of Environmental Health Research*, 2025.

In recent years, the health impacts of phthalates and bisphenol-A (BPA) have garnered significant research attention due to their widespread use in consumer products and identification as endocrine disrupting chemicals (EDCs). Human exposure occurs through various pathways, including dietary intake, inhalation of dust, and dermal contact. This study initially aimed to analyze serum samples from 200 participants in Jabalpur city (Central India); however, samples from 173 individuals were ultimately analyzed to assess the occurrence, concentration patterns, and gender-related differences of six phthalates and BPA. Serum samples were collected, processed, and analyzed for EDC content using gas chromatography coupled with mass spectrometry. The findings highlighted differences in detection frequencies among genders and residential areas, shaped by environmental exposure variability, lifestyle variations, and gender-specific metabolic disparities. All the targeted analytes were detected with diethyl phthalate (DEP) having the highest mean concentration of 13.74 +/- 6.2 ng/ml, followed by di(2-ethylhexyl) phthalate (DEHP) with mean value of 13.69 +/- 99.82 ng/ml in human serum. Studies have linked DEP exposure endocrine disruption and reproductive abnormalities. Subsequent research endeavors should prioritize elucidating EDC sources, pathways, and health impacts, facilitating evidence-based policies to mitigate risks and ensure a healthier future. https://doi.org/10.1080/09603123.2025.2502636

A systematic review of pre-analytical factors in urinary EDCs biomonitoring: Toward robust epidemiological studies,
Wu, L. X., Jiang, Y., Xie, S. S., Zhu, B. Q. and Ye, X. Q., *Microchemical Journal*, Jul 2025, Vol. 214.

Endocrine disrupting chemicals (EDCs) are chemicals in the environment that interfere with the endocrine function of humans or animals, potentially harming the health of intact organisms. Human biomonitoring assesses individual exposure risk by determining the level of EDCs in biological matrices. Detection of the risk of exposure to EDCs in populations is essential for epidemiologic studies, and urine is currently the most commonly used biological matrix in epidemiologic studies. During urine monitoring, many elements affect the accuracy of the assessment of EDCs, further contributing to bias in the associations between environmental exposures and health outcomes in epidemiologic studies. However, there are no studies that systematically analyze these factors and provide appropriate recommendations. We conducted a literature review focusing on the urine analysis procedures in epidemiologic studies. Relevant literature was retrieved from PubMed and the search equation was built from a combination of keywords, MeSH terms and Boolean operators. This search strategy identified 1437 articles, and after removing duplicates, only 77 were included in the study after title, abstract, and full-text screening. This study explained how to develop a urine sampling strategy and emphasized the need for cryopreservation of urine, timely testing, and avoidance of repeated freezing and thawing. The advantages and limitations of the different methods of pre-treatment and instrumentation during urine sample testing were comparatively elucidated, and the choice of methods in different situations was explained. Possible interferences such as background contamination and matrix effects also need to be considered throughout the monitoring process. This review contributes to the selection of methods for monitoring EDCs in urine for epidemiologic studies and provides a

theoretical basis for accurately assessing the level of exposure to EDCs.
https://doi.org/10.1016/j.microc.2025.113968

Analysis of Phthalate Monoesters and Bisphenols in Human Prostate Cancer Tissue and Urine, Zhang, T. N., Guo, J. Q., Sun, W. Y., Huang, X. Y., Zhang, Z. L., Jin, Y. M., Hu, Z. F., Qiu, S. and Zou, X. L., *Journal of Separation Science*, Apr 2025, Vol. 48, no. 4.

A growing concern has been raised about human exposure to phthalates and bisphenols, while data is limited regarding the accumulation of these endocrine disrupting chemicals at the target tissue. In this study, a novel, simple, and sensitive method was successfully developed for the simultaneous determination of nine phthalate monoesters and nine bisphenols in human prostate tissue samples. A solid-liquid extraction procedure was applied following ultra-high performance liquid chromatography tandem mass spectrometry analysis. The detection and quantification limits were in the range of 4.12 x 10-3 to 0.370 ng/g and 1.38 x 10-3 to 1.23 ng/g, respectively. The average spiked recoveries varied from 71.4% to 102%, with relative standard deviations <= 10%. Finally, this method was applied to 76 human prostate tissue samples. Four phthalate monoesters (mono-ethyl phthalate, mono-iso-butyl phthalate, mono-n-butyl phthalate, and mono-benzyl phthalate) were detected with the highest frequency of 98.68%, followed by other five phthalate monoesters (71.05% similar to 94.74%), bisphenol S (72.37%), and bisphenol A (57.89%). Five bisphenols were not detected in any tissue sample. The concentrations of detected phthalate monoesters and bisphenols ranged from 1.12 x 10-3 to 1.86 x 102 ng/g and 6.08 x 10-3 to 39.0 ng/g, respectively, with standard errors ranging from 3.25x10-3 to 4.64 ng/g. Besides, a positive correlation for the concentration of seven phthalate monoesters and bisphenol A could be observed between tissue and urine, which indicates that these metabolites in urine can serve as noninvasive biomarkers to evaluate the true exposure level of prostate tissue. This study provides data and information on exposure to phthalate monoesters and bisphenols in human prostate tissue and the association with their urinary metabolites, supporting further studies of pollutant exposure and prostate disease.
https://doi.org/10.1002/jssc.70154

Méthodes

The intracellular free concentration of endocrine disrupting chemicals enables translation between cell-free and cell-based estrogenic activity assays,
Kos, V. M., Arvidsson, S., Islam, B., Nikiforova, V., Mickols, E., Meyer, A., Svensson, R., Boztepe, U. G., Banti, E., Lundquist, P., Khalidi, H., Gardner, I., Spjuth, O., Cotgreave, I. and Artursson, P., *Environmental Toxicology and Pharmacology*, Aug 2025, Vol. 117.

Many environmental toxicants can activate estrogen receptor alpha (ER alpha), disrupting normal endocrine function. While these activities are predicted across in silico, in vitro, and in vivo models, translating active concentrations between these systems remains challenging. We hypothesized that cellular uptake and the resulting free intracellular toxicant concentration could bridge this gap. Using cell-free (hER) and cell-based (ER alpha-CALUX cells) estrogen assays, we tested this hypothesis by determination of the free intracellular concentration available for binding to the intracellularly located ER alpha. Predictive modeling identified three classes of estrogenic chemicals from the ToxCast collection: bisphenols, parabens, and phthalates. Experimental data confirmed potency differences of up to 100-fold between the cell-free and cell-based models. Cellular toxicokinetic (TK) parameters, including cellular uptake and intracellular binding, were determined using computational and experimental methods. Incorporating experimental TK parameters significantly improved the correlation between ER alpha activities in the cell-free and cellular models

(from r = 0.6230, P = 0.0989 without corrections to r = 0.8869, P = 0.0033 after corrections), and bridged the gap between the cell free and cell based assays. Both computational and experimental TK parameters varied widely across chemical classes and compounds. Correcting active concentrations for free intracellular levels enhanced assay correlations, with experimentally derived corrections showing the strongest improvement with r = 0.8869 (compared to the in silico derived corrections with r = 0.811). Our findings highlight the critical role of free intracellular concentration in determining the biological activity of estrogenic toxicants and emphasize its importance in accurately assessing their endocrine-disrupting potential.
https://doi.org/10.1016/j.etap.2025.104750

Testing the Development of a Diet-Based Bisphenol a Score to Facilitate Studies on Child Neurodevelopment: A Pilot Project,
Patti, M. A., Kivumbi, A., Rando, J., Song, A., Croen, L. A., Schmidt, R. J., Volk, H. E. and Lyall, K., *Int J Environ Res Public Health*, Jul 25 2025, Vol. 22, no. 8.

While gestational Bisphenol A (BPA) exposure has been associated with autism, limited work has focused on dietary sources. Here, we sought to develop a summary metric to capture dietary exposure specifically and test its associations with measured levels, as well as child traits related to autism. Participants (n = 116) were from the Early Autism Risk Longitudinal Investigation (EARLI) Study, which recruited pregnant women who previously had a child diagnosed with autism. Maternal concentrations of BPA were quantified in urine, and dietary sources of BPA were ascertained via food frequency questionnaires during gestation. A novel BPA "dietary burden score" was developed based on reported intake of foods known to contribute to BPA exposure (i.e., canned foods) from a Dietary History Questionnaire modified for pregnancy. Child autism-related traits were assessed via the Social Responsiveness Scale (SRS-2). We examined associations between BPA biomarkers, dietary burden scores, and child SRS scores. Dietary burden scores were weakly correlated with urinary BPA concentrations (R = 0.19, p = 0.05) but were not associated with child SRS scores. Our work suggests that more detailed dietary assessments may be needed to fully capture diet-based BPA exposures and address diet as a modifiable source of chemical exposure to reduce associated health impacts of BPA. https://doi.org/10.3390/ijerph22081174

Inter-laboratory validation study of an in vitro glucocorticoid receptor transactivation assay for testing potential endocrine disrupting chemicals,
Rivero-Arze, A., Grimaldi, M., Maillet, G., Gesbert, C., Michelin, E., Garoche, C., Maillot-Maréchal, E., Palluel, O., Sermier, F., Hoffmann, S., Couteau, J., Hubert, P., Grignard, E., Aït-Aïssa, S., Balaguer, P. and Österlund, T., *Toxicol In Vitro*, Dec 2025, Vol. 109, p. 106109.

The glucocorticoid receptor (GR) belongs to the family of steroid receptors (SRs). These receptors regulate a vast selection of cell-, tissue-, and organism biology, and are also targets of endocrine disrupting chemicals warranting design and validation of in vitro assays. Here we report a "blinded" ring trial of an in vitro cell-based GR transactivation assay with four involved laboratories. The laboratories set up the assay and tested 34 selected chemicals with remarkably good concordance. There was agreement between all laboratories for the classification of activity in 97 % of the cases, and three or more laboratories were always in agreement. The within laboratory concordance was very high (99.6 %) with only one of all 272 triplicates deviating. The assay was, thus, deemed easily transferable and reproducible within and between laboratories, since they would arrive at the same qualitative results. Furthermore, for the chemicals with solid data regarding GR activation or inhibition, the laboratories arrived at the expected conclusion in all cases. Overall, the transfer and validation were successful, and the method is under evaluation to become an OECD test guideline. The method is expected to become valuable in tiered approaches for assessing chemicals or

environmental samples together with other similar methods.
https://doi.org/10.1016/j.tiv.2025.106109

[Methodological monitoring of the effects of endocrine disruptors in complex health maintenance],
Sepp, K., Kiss, P. S., László, A., Valkusz, Z., Radács, M., Gálfi, M. and Molnár, Z., *Orv Hetil*, Aug 3 2025, Vol. 166, no. 31, p. 1209-1216.

Introduction: By the 3rd millennium, the Earth as a living environment had been altered by environmental stresses. For 25 years, our research group has been thematically engaged in model studies of homeostatic disruptor effects. These have enabled thematic studies to follow the effects of chemical agents, e.g., the combined effects of chlorobenzenes (hexachlorobenzene : 1,2,4-trichlorobenzene 1 : 1), which have endocrine disrupting properties. Objective: We aimed to develop a test model system to investigate the effects of endocrine disruptors in a validated test system. Method: In the test system, male and female Wistar rats were used as model animals for in vivo studies. Subtoxicity was controlled by liver enzymes and body weight and physiological characterization. The exposure pathway was standardized. Then, the organism-level sub-toxic dose range and the time windows for acute and chronic monitoring of subtoxicity were defined. Plasma arginine vasopressin, and oxytocin levels were measured by RIA and LIA. Data were evaluated using SAS and ANOVA. Results: A stable in vivo control system had to be established to monitor the biological effects. The chlorobenzene exposures were standardized via gastrointestinal probe, in a final volume of 1.0 ml per day, at doses of 0.1 and 1.0 µg/kg body weight. The chlorobenzene potency model compounds were optimized during in vivo gastrointestinal exposure. Exposures were standardized: via gastrointestinal probe, 1 ml final volume per day, at doses of 0.1 and 1.0 µg/kg body weight. Experimental time intervals were 0–90 days. Discussion: In our work, we have succeeded in developing a test system to establish a validated method for monitoring chemical environmental exposures. We have also developed a standardised procedure for the determination of human toxicity potentials. Conclusion: A validated test system has been developed to test for persistent organic pollutants, which are nowadays a major health concern, making their testing of real relevance in clinical practice. Orv Hetil. 2025; 166(31): 1209–1216.
https://doi.org/10.1556/650.2025.33353

Applying New Approach Methods for Toxicokinetics for Chemical Risk Assessment,
Wambaugh, J. F., Paul Friedman, K., Beal, M. A., Moffat, I., Hughes, M. F., Nong, A., Dorne, J. C. M., Ashraf, M. W., Barton-Maclaren, T. S., Devito, M., Ferguson, S. S., Judson, R. S., Long, A. S., Paini, A., Sampani, S., Thomas, R. S. and Wetmore, B. A., *Chem Res Toxicol*, Aug 18 2025, Vol. 38, no. 8, p. 1408-1441.

Toxicokinetic (TK) modeling provides critical information linking chemical exposures to tissue concentrations, predicting persistence in the body and determining the route(s) of elimination. Unfortunately, TK data are not available for most chemicals in commerce and the environment. To better understand and address these important information gaps, researchers and regulatory scientists from the international consortium of Accelerating the Pace of Chemical Risk Assessment herein present a flexible framework for characterizing the suitability of TK new approach methods (NAMs) to address chemical risk questions. High throughput toxicokinetics (HTTK) combines chemical-specific in vitro measures of TK with reproducible transparent and open-source TK models. HTTK supports the interpretation of data from in vitro bioactivity NAMs in a public health risk context and enhances the interpretation of biomonitoring data. A tiered framework has been developed focusing on two key aspects: (1) the regulatory decision context and (2) chemical properties and data. Differing levels of certainty are needed for relative risk prioritization,

prospective risk assessment, and for protecting susceptible populations. Here HTTK is described with respect to measurement and modeling applications, relevant decision contexts, applicable chemistry, value of information, and certainty of predictions. In some cases, quantitative structure-property relationship (QSPR) models exist as alternatives to measurement and are discussed when they are appropriate. A series of examples applying the decision trees in specific public health scenarios are provided to illustrate that writing short responses, prompted by the decision trees and supported by the discussion and references collected here, may provide defensible written justification for or against the use of HTTK. The framework is intended to serve as a guide to chemical regulators and risk assessors who are interested to know when and where HTTK might be used for public health safety or risk decision making and when further expert guidance is needed. https://doi.org/10.1021/acs.chemrestox.5c00161

Biomonitoring Xenobiotics in Human Biospecimens: Challenges, Advances, and the Future of Exposome Characterization,
Zhu, X. R., Tang, X. N., Ng, C., Li, L., Lai, Y. J., Miller, G. W., Jiang, C., Barchowsky, A., Buchanich, J. and Gao, P., *Reviews of Environmental Contamination and Toxicology*, Dec 2025, Vol. 263, no. 1.

Xenobiotics, defined as foreign chemical substances not normally produced by or expected to be present in an organism, are pervasive throughout the human body system. While some xenobiotics have known adverse health effects, the impact of many remains unclear, particularly when considering the potential synergistic or additive effects of chemical mixtures. Human biomonitoring, using biospecimens such as blood, urine, placenta, umbilical cord blood, stool, milk, sweat, saliva, tears, teeth, hair, nails, breath, and cerebrospinal fluid, is a common approach to assess xenobiotic exposure. However, these matrices have inherent limitations in accurately measuring the vast array of chemicals constituting the human chemical exposome-the entirety of chemical exposures an individual experiences over time. This comprehensive review critically analyzes the advantages and limitations of both invasive and noninvasive biospecimens used in human biomonitoring. We outline major classes of detectable xenobiotics in these matrices, compare their qualitative and quantitative feasibility, and discuss challenges in using biospecimens to monitor the internal chemical exposome. The review highlights the importance of integrating complementary external monitoring methods alongside biospecimen analysis, given the short half-lives and trace levels of some xenobiotics in accessible biospecimens. We also discuss emerging technologies and methodologies in biomonitoring, including advanced analytical techniques, wearable sensors, and multi-omics approaches. Additionally, we discuss the ethical, legal, and social implications of biomonitoring and external monitoring. By synthesizing current knowledge and identifying research gaps, this review provides a comprehensive overview of xenobiotics in human biospecimens and outlines future directions for better characterizing the human chemical exposome. These insights are crucial for advancing our understanding of xenobiotic exposures and their health impacts, ultimately informing more effective strategies for disease prevention and intervention. https://doi.org/10.1007/s44169-025-00088-2

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

ECHA publishes updated PFAS restriction proposal / Timeline for PFAS restriction evaluation announced,
ECHA (aout 2025),

The European Chemicals Agency (ECHA) has published the updated proposal to restrict per- and polyfluoroalkyl substances (PFAS) under the EU's chemicals regulation, REACH. The update has been prepared by the authorities from Denmark, Germany, the Netherlands, Norway and Sweden, who submitted the initial proposal in January 2023.
The five authorities, acting as the Dossier Submitter, have completed their evaluation of the more than 5 600 scientific and technical comments received from third parties during the 2023 consultation. Based on the evidence gathered, they have updated their initial restriction proposal. This updated report, called the Background Document, forms the basis for ECHA's committees' opinions. This document may still be updated further, based on the evaluation of the committees.
https://echa.europa.eu/hot-topics/perfluoroalkyl-chemicals-pfas#msdynmkt_trackingcontext=4d7029c5-ca2f-4104-bb9f-a0787db50000

Etablissements de santé et perturbateurs endocriniens
(2025). ARS.
Appel à projets pour soutenir des actions portées par les établissements de santé (avec services de maternité et/ou néonatologie) et visant à la réduction de l'exposition aux perturbateurs endocriniens de la femme enceinte et du jeune enfant au sein et en dehors de l'établissement.,
https://www.auvergne-rhone-alpes.ars.sante.fr/etablissements-de-sante-et-perturbateurs-endocriniens

EU Guidance for transitioning to Fluorine-Free Firefighting Foams,
ECHA (2025),
This guideline is prepared by the European Commission, in collaboration with the European chemicals Agency and experts from EU countries. This guidance aims to support stakeholders in the transition from PFAS-containing firefighting foams to fluorine-free alternatives in line with upcoming per- and polyfluoroalkyl substances (PFAS)-related regulatory requirements under the POPs Regulation and REACH. This document consolidates existing guidance on best practices, technical challenges, and feasible solutions to facilitate compliance with these regulations. It provides information on available fluorine-free alternatives, methodologies for detecting and mitigating PFAS residues, and recommendations for environmentally sound disposal practices.
https://echa.europa.eu/documents/10162/6956102/EU_guidance_for_transitioning_to_fluorine-free_firefighting_foams_en.pdf/24d79e79-a1af-dd0c-0b31-bdc2f78f08fe#msdynmkt_trackingcontext=99e7c4fd-075d-4f8f-9a46-a2b2fa760300

Perturbateurs endocriniens : les esthéticiennes dans la difficulté avec des stocks de vernis interdits,
France Info, 8 septembre 2025.

Depuis le 1er septembre, les esthéticiennes se rongent les ongles : certains vernis contenant des perturbateurs endocriniens sont interdits d'utilisation. Le problème, c'est que certains fournisseurs se sont bien gardés de prévenir les salons de beauté. https://doi.org/https://france3-regions.franceinfo.fr/bourgogne-franche-comte/saone-et-loire/le-creusot/perturbateurs-endocriniens-les-estheticiennes-dans-la-difficulte-avec-des-stocks-de-produits-interdits-3212999.html

Replay Webinaire : Communicating about EDCs & Health: Why words matter,
CHE Collaborative for Health and Environment (juillet 2025),
Exposure to endocrine disrupting chemicals (EDCs) can affect every aspect of human life, including sexual development, neurodevelopment, and metabolic health. Scientists working to understand and address the effects of EDCs on human health sometimes face difficult choices about how to

communicate the results of their work. In this webinar, Dr. Kevin Elliott and Dr. Laura Vandenberg discussed the range of ways in which scientists can present information on research findings. They explained how a given frame can have both beneficial and harmful effects. For example, framing an EDC-related health outcome as a disease or disability can help to focus public attention on hazards of toxic chemicals and promote action to protect human health. At the same time, this framing can be used to stigmatize and harm individuals and communities. The speakers shared a range of strategies available to researchers to communicate responsibly and effectively.
http://healthandenvironment.org/che-webinars/96990

Webinaire - Perturbateurs endocriniens : les repérer pour prévenir les risques en entreprise - Rendez-vous le 21 novembre 2025 à 11 heures,
INRS (novembre 2025),
Comment repérer et inventorier les perturbateurs endocriniens et les produits qui en contiennent en milieu professionnel ? Quels outils utiliser ? Quelles sont les sources et les situations d'exposition ? Quelles sont les grandes lignes de la démarche de prévention ? Pour répondre à ces questions, l'INRS organise le 21 novembre 2025 un webinaire destiné à tous ceux qui souhaitent identifier et repérer les perturbateurs endocriniens dans leur entreprise, afin de mettre en œuvre des mesures de prévention adaptées. https://www.inrs.fr/footer/agenda/webinaire-perturbateurs-endocriniens-21-11-2025.html

Food-Borne Endocrine-Disruption: An EU Risk Governance Perspective,
El Gemayel, M., *European Journal of Risk Regulation*, 2025.

Exposure to endocrine disrupting chemicals is linked to negative health impacts, including non-communicable diseases such as obesity, cardiovascular diseases and cancer. This disease burden compromises consumer safety and costs the European Union an estimated 163 billion per year. Given these stakes, the importance of effectively regulating EDCs in food is paramount. Yet regulators face difficult challenges: scientific uncertainty, the ubiquity of EDCs in food products, and pressure from economic and political interests all complicate legislative responses. From a risk regulation perspective, the core problem is how to protect public health from EDC risks in food amidst these uncertainties and constraints. This paper addresses the problem by examining the current EU regulatory framework for managing EDCs in the food supply chain, identifying gaps and weaknesses, and proposing improvements to better safeguard public health. From this risk regulation perspective, the paper highlights the benefits of ensuring regulatory action keeps pace with scientific evidence, leveraging the General Food Law Regulation for a comprehensive approach to EDCs, and developing sector-specific EDC regulation across the food supply chain.
https://doi.org/10.1017/err.2025.10017

A review of microplastic pollution and human health risk assessment: current knowledge and future outlook,
Hoang, H. G., Nguyen, N. S. H., Zhang, T., Tran, H. T., Mukherjee, S. and Naidu, R., *Frontiers in Environmental Science*, Jun 18 2025, Vol. 13.

The rapid growth of the global population, coupled with the expansion of industrial, agricultural, commercial, and service activities, has led to a significant increase in microplastic contamination in aquatic environments. An estimated 265 million metric tons of plastic waste are produced globally each year, with about 4.8-12.7 million metric tons ending up in the ocean. Microplastics can infiltrate the food chain or come into contact with humans through the skin, eventually penetrating and accumulating in the body. Globally, individuals are estimated to consume between 11,845 and 193,200 microplastic particles per year, with drinking water identified as the primary source. The

toxicity of microplastics stems from both their inherent properties and their ability to interact with other pollutants, such as heavy metals. Adverse health effects linked to microplastic exposure include metabolic disruptions, transport to internal organs, inflammatory responses, oxidative stress, cytotoxicity, and potential damage to the nervous and reproductive systems, along with possible carcinogenic outcomes. Despite these concerns, there are currently no standardized methods for assessing the human health risks associated with microplastic exposure. There is a critical need for in-depth research to clarify the toxicological impacts and health risks of microplastics, along with the development of reliable risk assessment frameworks. This review seeks to present a comprehensive summary of microplastic levels in aquatic systems, their possible effects on human health, and the methodologies currently used to assess these risks.
https://doi.org/10.3389/fenvs.2025.1606332

Assessment of endocrine disruptors in the European Union: Current regulatory framework, use of new approach methodologies (NAMs) and recommendations for improvements,
Holmer, M. L., Holmberg, R. D., Despicht, C., Bouftas, N., Axelstad, M., Beronius, A., Zilliacus, J., Van Duursen, M. and Svingen, T., Regulatory Toxicology and Pharmacology Volume 162, November 2025

Exposure to endocrine disruptors (EDs) are associated with significant risks to human health and the environment. The European Union (EU) thus prioritizes their identification and regulation and is developing a roadmap to phase out animal testing in chemical safety assessments while advancing New Approach Methodologies (NAMs). This review outlines EU's practices for ED identification, focusing on the use of NAMs, as well as Defined Approaches and read-across. We assessed the current EU framework under the Classification, Labelling and Packaging (CLP) Regulation, the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), the Plant Protection Products Regulation (PPPR), and the Biocidal Products Regulation (BPR), evaluating current use of NAMs and reflection on potential future use. We find that EU legislation and guidance documents allow the use of NAMs in ED identification, including for assessment of endocrine activity and adversity. However, guidance on predicting adversity using NAMs remains limited, and ED identifications have largely depended on animal data to assess endocrine-mediated adversity. Continued in vivo testing until reliable methodologies are accepted as alternatives and routinely applied is required. The report concludes with short- and long-term recommendations for updates to the information requirements across regulations and further development of methods to predict endocrine-mediated adversity. https://doi.org/10.1016/j.yrtph.2025.105883

Global research on endocrine disruptors as emerging hazards for human health and the environment,
Klingelhöfer, D., Braun, M., Dröge, J., Brüggmann, D. and Groneberg, D. A., *Frontiers in Endocrinology*, Jun 26 2025, Vol. 16.

Endocrine disruptors (EDs) contaminate nearly every ecosystem and are significantly associated with different neurological and neurodevelopmental disorders. To date, there is no comprehensive literature on global publication efforts. Since there are many unknown substances, modes of action, and risks of EDs, it is necessary to provide detailed insight into global publication patterns from temporal, regional, and socioeconomic perspectives. Hence, this review article provides background information for all stakeholders, from scientists to clinicians and policymakers. A disproportionate increase in research activity was observed, mainly from the USA and China, with a strong north-south divide. Multi-disciplinarity is characteristic, with a trend toward an ecological focus. Low- and middle-income economies are underrepresented in research on EDs. Therefore, global research needs to be refocused and expanded to more global approaches that take inspiration from the few

successful collaborations with their synergistic effects.
https://doi.org/10.3389/fendo.2025.1561711

Next generation risk assessment and new approach methodologies for safe and sustainable by design chemicals and materials: Perspectives and challenges for occupational health,
Leso, V., Nowack, B., Karakoltzidis, A., Nikiforou, F., Karakitsios, S., Sarigiannis, D. and Iavicoli, I., *Toxicology*, Nov 2025, Vol. 517, p. 154211.

Europe is facing increasingly challenging threats to health and well-being, including chemical pollution, climate change, and biodiversity loss. To counter such threats, the European Union has developed a series of policy strategies, including the Chemicals Strategy for Sustainability and the Zero Pollution Action Plan that pointed out the need for safe-and-sustainable-by-design (SSbD) chemicals/materials. The SSbD and the "zero pollution" ambition will inevitably lead to a transformation of the conditions of exposure to chemicals both in general living environments and workplaces with the consequent need to adequately anticipate and manage the chemical risk, starting from the assessment of the hazard and risk characterization. Among those, next generation risk assessment (NGRA) is defined as a human-relevant, exposure-led, hypothesis driven risk assessment approach, designed to prevent harm. To date, application of NGRA has been restricted to assessing the use of cosmetics, and it has not been implemented in occupational risk assessment. Occupational safety assessment represents an area that would benefit from increasing application of NGRA to safety decision making. Additionally, the application of new approach methodologies (NAMs) can support the generation of data useful to implement the operationalization of the SSbD framework, favorably impacting the adoption of suitable management strategies. In turn, the historical occupational preventive and protective approach to the health and safety of workers may provide support to adequately implement NGRA in the occupational context. Therefore, this work aims to provide an overview on the principal available NAMs and their possible implications for occupational chemical risk assessment and management.
https://doi.org/10.1016/j.tox.2025.154211

Does my patient need testing for PFAS 'forever chemicals'?,
Zuccaro, P., Valvi, D. and Vasiliou, V., *Cleve Clin J Med*, Aug 1 2025, Vol. 92, no. 8, p. 463-465.
https://doi.org/10.3949/ccjm.92a.24082

Toxicité sur les animaux

The environmental contaminants, tributyltin and bisphenol S, alone or in combination, harm the hypothalamus-pituitary-gonadal axis and uterus,
Anselmo, D. D., Azeredo, D. B. C., Röpke, R., Jr., Souza, L. L. D., Lisboa, P. C., Graceli, J. B., Gitirana, L. D., Ferreira, A. C. F., Paiva-Melo, F. D. and Miranda-Alves, L., *Molecular and Cellular Endocrinology*, Aug 1 2025, Vol. 605.

Endocrine disrupting-chemicals (EDCs) are chemical compounds found in the environment that can have adverse impacts on human health. Among these agents are tributyltin (TBT) and bisphenol S (BPS). TBT is used in antifouling paints, and its indiscriminate use has health repercussions. BPS is found in plastic products and marketed as a safe alternative to bisphenol A (BPA). Little is known about the effects resulting from interactions between different EDCs on the organisms. The aim of this study was to analyze changes induced by exposure to these compounds in hypothalamic-

pituitary-gonadal (HPG) axis and uterus. We divided four groups: Control, TBT 100 ng kg- 1.day- 1, BPS 50 mu g kg- 1.day- 1, and the group simultaneously exposed to TBT and BPS. Rats were gavaged for 15 days and euthanized in the estrus phase. All EDCs groups showed uterus with cellular hyperplasia, glandular degeneration, increased epithelial thickness, and vacuolization. In the ovaries, there was an increase in atretic follicles in all EDCs groups. In the hypothalamus, the group exposed to the mixture showed an increase in the GnRH gene. In the blood, all EDCs groups had reduced levels of FSH and LH. Additionally, the BPS and mixture groups exhibited reduced levels of prolactin. Therefore, we suggest that exposure to these agents may contribute to damage to the female reproductive system, and that doses considered safe by regulatory agencies need to be reassessed. https://doi.org/10.1016/j.mce.2025.112558

Developmental neurotoxicity of bisphenol F and bisphenol S in animal model systems: A literature review,
Cantua, R. and Mulligan, K., *Neurotoxicology*, May 2025, Vol. 108, p. 263-280.

Neurodevelopmental disorders have complex etiologies, stemming both from genetic and environmental risk factors, including gestational exposure to bisphenol A (BPA). BPA is an endocrine-disrupting chemical widely used in the synthesis of plastics and epoxy-resins. In 2012, the Food and Drug Administration issued a ban on the use of BPA in certain baby and childhood products, which contributed to the proliferation of BPA-free products. To make products without BPA, plastic and epoxy manufacturers often use chemical analogs, including bisphenol F (BPF) and bisphenol S (BPS). However, the structural and biochemical similarities BPF and BPS share with BPA suggest they may have similar molecular and cellular impacts on the developing nervous system, despite consumers generally regarding BPA-free products as safer alternatives. In this review, we synthesized all available peer-reviewed primary literature to date reporting on the neurodevelopmental impacts of BPF and/or BPS in animal models. In total, 61 papers were identified as relevant to the topic, including evaluation of BPF- and BPSassociated neurodevelopmental phenotypes such as changes in neurodevelopmental gene expression, the proliferation and differentiation of neural stem cells, synaptogenesis, central nervous system morphology, neuronal cell death, and behavior. Though less extensively studied than BPA, the collective works described here indicate that BPF and BPS can act as developmental neurotoxicants in animal models, urging further mechanistic and epidemiological analyses of these bisphenol analogs, as well as a reconsideration by regulatory agencies of policies surrounding their usage. https://doi.org/10.1016/j.neuro.2025.04.008

Perinatal bisphenol A exposure impairs gut microbial colonization: Implications for offspring obesity and neurodevelopment,
López-Moreno, A., Torres-Sánchez, A., Suárez, A., Ruiz-Rodríguez, A. and Aguilera, M., *Ecotoxicology and Environmental Safety*, Jun 15 2025, Vol. 298.

Exposure to plasticiser xenobiotics such as BPA has emerged as a significant health challenge due to globalised and industrial packaged food production. Toxicological approaches in animal models have revealed complex effects, using variable doses of BPA, on reproduction, development, obesity, immune function, metabolic and systemic toxicity. Besides, gut microbiota has emerged as a key player in regulating the impact of xenobiotic exposure on host metabolism. The effect that BPA may exert on the gut microbiota and its consequences for the host's health remains unclear. Exposure to BPA during the perinatal period requires special attention and prevention approaches since it is a particularly vulnerable period and highly implicated in the metabolic health of childhood and adulthood. The aim of this study was to assess the effects of the BPA administration during the perinatal period on promoting obesity phenotypes, altering the composition of the gut microbiota

and neurocognitive development of the offspring in a murine model. In this study, pregnant mice and their offspring were administered BPA, and the increase in weight and fat accumulation, the gut microbiota composition, and the cognitive development of the offspring were analyzed. In addition, a high-fat diet (HFD) was given to the mice to test for the synergistic obesogenic effect of BPA. Our results demonstrated that BPA exposure impaired the natural remodelling of the gut microbiota during pregnancy. For instance, Akkermansia and Prevotellaceae decreased during natural remodelling of the gut microbiota during pregnancy, but they did not change in the BPA-exposed pregnant mice. Conversely, several members of the Dubosiella genus increased during normal pregnancy but not in BPA-exposed pregnant mice. Moreover, BPA exposure and HFD differentially affect gut microbial transfer from mothers to offspring and both synergistically impact the gut microbiota's establishment in the offspring. Perinatal BPA exposure imprinted changes during colonisation and maturation process of the offspring gut microbiota, identifying Lactobacillus, Eubacterium and Acetatifactor as signature genera enriched in BPA and BPA-exposed mice fed with HFD, taxa involved in a more efficient at energy harvesting from the diet. Moreover, perinatal BPA exposure seemed to alter fat and lean percentages and triggered Muribaculacea taxa imbalance that appears to be associated with disrupted activity, spatial learning, and memory, mimicking impulsivity and hyperactivity-like behavior in the offspring. In conclusion, BPA exposure and HFD exert an influence on the vertical transfer of gut microbiota from mothers to offspring and drive towards an altered establishment of gut microbiota taxa in early life, contributing to enhancing susceptibility to obesity and behavioural disorders. https://doi.org/10.1016/j.ecoenv.2025.118295

In vitro effects of environmentally relevant concentrations of nonylphenol and selected pyrethroid metabolites on a mouse sertoli cell line (TM4),
Matjomane, N. K., Repsold, L., Patrick, S. M., Van Zijl, M. C., Visagie, M. H. and Aneck-Hahn, N. H., *Toxicology Mechanisms and Methods*, 2025.

Advances in the chemical industry and increased environmental pollution have contributed to declining reproductive health. Many pollutants act as endocrine-disrupting chemicals (EDCs), with (anti-)estrogenic and (anti-)androgenic properties that disrupt hormonal balance and contribute to male reproductive dysfunction. Mouse Sertoli cells, which closely resemble human Sertoli cells, are targets for various environmental contaminants, making the cell line an ideal model for male reproductive toxicological studies. Sertoli cells (TM4) were exposed to environmentally relevant concentrations of EDCs, including cypermethrin, deltamethrin, rac-trans permethrinic acid, 3-phenoxybenzoic acid and para-nonylphenol (p-NP), for 24 h in vitro. Cytotoxicity was measured using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay, oxidative stress via an intracellular total reactive oxygen species (ROS) activity assay kit, and morphological changes via hematoxylin & eosin staining. The MTT assay revealed a moderate decrease (approximately 20% cell death) in cell viability. ROS levels were significantly higher in EDC-treated cells than in controls, with small effect sizes confirmed through Cohen's d analysis. Morphological changes, including membrane elongation, cytoplasmic vesicles, and reduced cell density, were most pronounced in p-NP-exposed cells. These findings suggest that exposure to pyrethroids and nonylphenol may induce toxicity in mouse Sertoli cells. https://doi.org/10.1080/15376516.2025.2528100

Exposure to brominated flame retardants during pregnancy and lactation increases the prevalence of breast lesions and cancer-associated pathways in sprague-dawley rats,
Mcdermott, A., Juárez, M., Wade, M. G., Patten, S. A. and Plante, I., *Reproductive Toxicology*, Aug 2025, Vol. 135.

The mammary gland undergoes significant changes during pregnancy, lactation, and involution, making it highly susceptible to endocrine-disrupting chemicals such as brominated flame retardants

(BFRs). Despite being restricted in many countries, some BFRs persist in the environment and accumulate in human tissues, including the mammary gland and human milk. This study investigates the effects of BFRs exposure during pregnancy and lactation on mammary gland development and breast cancer risk in a rat model. Dams were exposed to a mixture of polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecane (HBCDD), formulated based on relative congener levels found in house dust. Post-weaning, dams were treated with 7,12-dimethylbenz[a] anthracene (DMBA) to initiate tumor formation. The results revealed that both low and high doses of BFRs induced lesions in mammary epithelium, with an increase in total lesion number in low dose. Molecular analysis revealed disruptions in the Wnt/(3-catenin signaling pathway, leading to an increase in oncogene expression, including c-Myc and c-Jun. RNA sequencing also indicated dysregulation in calcium signaling and glucose metabolism pathways. Our findings suggest that BFR exposure during the critical window of mammary gland involution compromises the cancer-protective effects of pregnancy and lactation. These effects are particularly significant at low exposure levels, demonstrating a non-monotonic dose-response. The study underscores the potential long-term health risks associated with environmental BFR exposure and highlights the need for further research on its implications on the risks of developing breast cancer later in life. https://doi.org/10.1016/j.reprotox.2025.108928

Assessing placental transfer and in utero reproductive effects in rats of a short-chained paraffin with in vitro endocrine disrupting properties,
Melchiors, M., Rosenmai, A. K., Cariou, R., Pedersen, M., Christiansen, S. and Svingen, T., *Current Research in Toxicology*, 2025 2025, Vol. 8.

Chlorinated paraffins (CPs) are industrial chemicals detected widely in the environment and human tissues, raising concerns due to their persistence, bioaccumulation, and potential health risks. CPs with lower chlorination or shorter carbon chain lengths can cross the placenta and have been detected in breast milk, indicating fetal and early postnatal exposure. Both in vitro and in vivo studies suggest that CPs exhibit endocrine-disrupting properties, particularly affecting reproductive development. This study investigates the developmental effects and placental transfer of 1,2,9,10-tetrachlorodecane (T4C10), a short-chained CP congener, by exposing pregnant rats from gestation days 7 to 21. T4C10 concentrations were measured in fetal and maternal blood, fetal steroid hormone levels were measured, and targeted gene expression was analyzed in the fetal genital tubercle. Despite prior in vitro evidence of endocrine-disrupting activity, in vivo exposure to T4C10 did not significantly affect reproductive parameters, including the anogenital distance (AGD), fetal steroid hormone profiles, or expression of androgen-and estrogen-regulated genes in the developing genital tubercle. The low systemic T4C10 levels in maternal and fetal blood suggest rapid metabolism or sequestration in adipose tissue, supported by increased liver weight in the exposed dams. These findings suggest that while T4C10 can cross the placenta, its bioavailability in vivo may be insufficient to elicit measurable endocrine-disrupting effects on reproductive development. This study underscores the importance of accounting for toxicokinetics when extrapolating in vitro findings to in vivo endpoints. https://doi.org/10.1016/j.crtox.2025.100237

Effects of carbamazepine-exposure on rat epididymal sperm in parental (F0) and F1 generations,
Nunes, M., De Britto, C. C., Freitas, R. D. D., Oliveira, A. S., Fischer, L. W., Miraglia, S. M. and De Oliva, S. U., *Reproductive Toxicology*, Sep 2025, Vol. 136.

Carbamazepine (CBZ) is a medication used for neurological and psychiatric disorders treatment. Its potential side effects on male reproduction are a cause for concern. Alterations in sperm parameters and sex hormone levels have been reported during and after prolonged therapy with CBZ. However, alterations in sperm quality are not necessarily associated with a decrease in fertility, and may

potentially lead to adverse effects on the offspring. The study aimed to evaluate the qualitative and quantitative parameters of epididymal sperm in CBZ-treated adult rats from pre-puberty to adulthood (F0 generation) and their potential impact on the spermatozoa of their offspring (F1 generation). Male rats were treated with CBZ (20 mg/Kg/day), administered by gavage, from pre-puberty (23 postnatal days-pnd) until adulthood (95pnd). The control group received olive oil (vehicle) following the same experimental procedure. At 95pnd, sperm qualitative and quantitative parameters were analyzed in the F0 and F1 generations. Measurements of testicular and epididymal malondialdehyde levels and plasma testosterone levels were also performed. Paternal chronic CBZ exposure (F0 generation) reduced sperm motility and viability, increased DNA fragmentation, and altered mitochondrial activity and acrosome integrity. Testosterone levels, testicular step 19 spermatid and daily sperm production also decreased. Significant increases in oxidative stress in the testis and epididymis were observed. These alterations also occurred in the F1 generation. The results suggest that prolonged paternal exposure to CBZ can cause sperm qualitative and quantitative alterations, decrease in testosterone levels, affecting intergenerationally the male reproductive health of offspring. https://doi.org/10.1016/j.reprotox.2025.108981

Gestational and Lactational Exposure to Perfluorohexanoic Acid Affects Behavior in Adult Male Mice: A Preliminary Study,
Plunk, E. C., Manz, K. E., Gomes, A., Pennell, K. D., Sobolewski, M. E. and Majewska, A. K., *European Journal of Neuroscience*, Jul 2025, Vol. 62, no. 1.

Legacy per- and polyfluoroalkyl substances (PFAS) have been associated with increased risk for male-biased neurobehavioral disorders. Industries have effectively replaced them with next-generation PFAS, including perfluorohexanoic acid (PFHxA). Zebrafish studies indicate developmental effects of PFHxA exposure on activity levels; however, the developmental neurotoxicology (DNT) of PFHxA has not been characterized in mammals. Human data reflect the need for mammalian DNT evaluations because PFHxA is found in the serum of pregnant women and in breast milk. Furthermore, postmortem studies show that PFHxA enters the brain, with the cerebellum having particularly elevated concentrations. Given this targeted brain region, we predicted that behavioral effects of PFHxA may target motor domains. To evaluate the effects of developmental PFHxA exposure, we exposed pregnant C57BL/6J mice daily from gestational day 0 through postnatal day (P)21 to vehicle (ddH2O), a lower (0.32 mg/kg of body weight [bw]) or a higher (50 mg/kg of bw) dose of PFHxA. Although this resulted in increases in the brain at P1 in the higher exposure group and in P21 in both exposure groups, by P90, PFHxA levels returned to those in control mice. We observed male-specific effects in the open-field test, the elevated plus maze, and the novel object recognition test in adulthood, with no overt effects in the hang test, inverted screen test, and gait scan. These preliminary findings indicate that PFHxA exposure may cause long-lasting changes in many behavioral domains in a mammalian model, and more research is needed to expand these evaluations to other cognitive domains. https://doi.org/10.1111/ejn.70174

Dye intermediates N-phenyl-2-naphthylamine and o-tolidine are novel environmental androgens with reproductive toxicity in male rats,
Shangguan, Z. H., Yang, K. Q., Pan, Q., Hu, H. L. and Wang, P., *Reproductive Toxicology*, Sep 2025, Vol. 136.

Endocrine disruptors are environmental chemicals that can interfere with the endocrine system. However, research on endocrine disruptors that interfere with androgen action is still limited. In this study, two new environmental androgens were identified. N-Phenyl-2-naphthylamine (PNA) and o-tolidine are dye intermediates widely used in industry to produce organic pigments. We found that both PNA and o-tolidine activated androgen receptor (AR) transcriptional activity in the luciferase

reporter assay and bound to AR-ligand binding domain directly in the surface plasmon resonance analysis. In vivo studies showed that PNA and otolidine induced the proliferation of seminal vesicle cells and increased seminal vesicle weight in immature male rats, indicating that these two compounds had androgenic activity in vivo. In addition, in mature male rats, PNA and o-tolidine reduced sperm concentration and motility and increased sperm deformities, and caused atrophy of the seminiferous tubules of the testis and decreased testosterone levels. These results suggest that PNA and otolidine are novel environmental androgens, which bind and activate AR and have toxicological effects on male reproductive function.
https://doi.org/10.1016/j.reprotox.2025.108955

Bayesian benchmark dose modeling analysis and derivation of points of departure for female reproductive toxicity following exposure to di(2-ethylhexyl) phthalate (DEHP) - effects on reproductive hormones, folliculogenesis and estrous cyclicity,
Silva, A. V., Tarvainen, I., Öberg, M., Laws, M., Hannon, P., Flaws, J. and Damdimopoulou, P., *Toxicological Sciences*, 2025.

Endocrine-disrupting chemicals such as di(2-ethylhexyl) phthalate (DEHP) pose significant risks to human reproductive health. However, regulatory frameworks often lack sufficient data on sensitive female-specific reproductive endpoints. This study investigates the sensitivity of hypothalamic-pituitary-ovarian (HPO) axis endpoints to DEHP exposure in adult female mice, applying Bayesian Benchmark dose (BBMD) modeling for dose-response assessment and derivation of points-of-departure (PODs) for risk assessment. Data from four studies where sexually mature female mice were exposed to DEHP (0.02 to 240 mg/kg bw/d) for 10 or 30 d via oral administration, or 30 d via diet, was modeled. Endpoints included ovarian follicle counts, serum hormones, estrous cyclicity, body, and organ weights. Results revealed dose-dependent changes and greater sensitivity of progesterone, ovarian follicle counts, and uterine weight, compared with estrous cyclicity, body weight, and other organ weights. For 10- and 30-d oral administration studies, the lowest nonzero BBMDLs were observed for serum progesterone levels (9.1 mg/kg bw/d) and primary follicle counts (19.5 mg/kg bw/d), respectively. These PODs were notably lower than most No-Adverse-Effect-Levels in the European Chemicals Agency's (ECHA's) "Registered substances factsheet" and "ECHA CHEM" databases. The majority of the studies derived PODs based on male (reproductive) endpoints. Finally, a derived no-effect level of 0.064 mg DEHP/kg bw/d was estimated, based on the overall lowest BBMDL, serum progesterone levels of the 10-d oral study. In conclusion, our study indicates that current guidelines may not fully capture reproductive risks for females, underscoring the need to refine regulatory endpoints to better protect female reproductive health in the context of DEHP exposure. https://doi.org/10.1093/toxsci/kfaf052

In Utero Exposure to 2,3,7,8-Tetrachlorodibenzo-p-dioxin Impairs the Ability of Mice to Clear a Pseudomonas aeruginosa Infection in Adulthood,
Stephens, V. R., Bohannon, J. K., Bruner-Tran, K. L., Davis, X. D., Oliver, M. A., Mcbride, M. A., Ameli, S., Rumph, J. T., Gaddy, J. A., Sherwood, E. R. and Osteen, K. G., *Microbiology Research*, Apr 26 2025, Vol. 16, no. 5.

Exposure to endocrine-disrupting chemicals (EDCs) has been linked to several pathologies in human health, especially those involving the immune system. The vast majority of studies have focused on cells and functions of the adaptive immune system with little investigation of the impact of EDCs on innate immunity. While EDC exposure remains a threat throughout the lifetime of an individual, the most detrimental effects on human health occur during critical stages of development, such as in utero. Fetal development is not only associated with growth and tissue remodeling but also with the establishment of key processes, including those of the immune system. Unfortunately, due to fetal

plasticity, developmental exposure to certain EDCs, including 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), can affect mammalian health well into adulthood by altering fetal programming. Herein, we hypothesize that in utero exposure to TCDD induces developmental reprogramming of the innate immune system that subsequently impacts the adult response to infection. To interrogate our hypothesis, we challenged adult mice with and without a history of in utero TCDD exposure with 1 x 108 CFU Pseudomonas aeruginosa via intraperitoneal injection. Results revealed a significant decrease in the number of innate leukocytes at the site of infection six hours after inoculation in toxicant-exposed mice compared to unexposed mice. The reduction in the number of phagocytes correlated with a reduction in bacterial clearance in toxicant-exposed mice. We also noted a decreased ability of peritoneal immune cells from toxicant-exposed mice to produce chemokines necessary for immune cell recruitment. Taken together, our results indicate that in utero EDC exposure impairs the innate immune response to a bacterial infection in adult offspring, particularly in males. https://doi.org/10.3390/microbiolres16050091

Pubertal atrazine exposure promotes adipocyte hypertrophy and hepatic steatosis in adult mice on a high-fat diet,
Teleken, J. L., Conte, I. C. M., Schorr, G., Glugoski, L., Bergenthal, L., Alves, J. L., Vicari, V. N., Vicari, M. R., Ribeiro, R. A. and Bonfleur, M. L., *Drug and Chemical Toxicology*, 2025.

The herbicide atrazine (ATZ) has been implicated in metabolic disruptions. This study investigated the long-term consequences of pubertal ATZ-based herbicide exposure on the development of obesity in mice fed a high-fat diet (HFD) in adulthood. Male and female C57Bl/6 mice received ATZ (5 mg/kg) or water (control group) from postnatal day (PND) 30 to 60. Following puberty, all mice were fed a HFD for 90 days. Pubertal ATZ-based herbicide exposure increases food intake, specifically in male mice. While body weight, subcutaneous adiposity, and white adipose tissue (WAT) weights remained unchanged, ATZ-exposed male mice showed worsened adipocyte hypertrophy and upregulation of genes involved fat metabolism (Srebp-2, Ppar-gamma, Cd36, and Adrp) in perigonadal WAT. Additionally, pubertal ATZ exposure exacerbated hepatic steatosis in both sexes, with increased ectopic fat accumulation in females correlating with increases in genes involved in fatty acid uptake and exportation (fatty acid transport protein 5 and microsomal triglyceride transfer protein). These findings provide new insights into the long-term metabolic consequences of pubertal exposure to ATZ, including exacerbated HFD-induced adiposity and hepatic steatosis. The observed sex-specific effects underscore the importance of considering pubertal windows of susceptibility to environmental disruptors and their potential impacts on adult health. https://doi.org/10.1080/01480545.2025.2534714

Bisphenol A exposure induces polycystic ovarian syndrome phenotype B and reduces fertility in adolescent female rats,
Zhang, W. J., Huang, R. F., Chen, J. H., Ren, L. L., Wang, L., Chen, Q. H. and Zhou, W. D., *Reproductive Biomedicine Online*, Jul 2025, Vol. 51, no. 1.

Research question: Does adolescent exposure to bisphenol A (BPA) induce polycystic ovary syndrome (PCOS)-like phenotypes in female rats? Design: Adolescent Sprague-Dawley rats (6-8 weeks old) were administered BPA (50 mg/kg body weight) in corn oil, or corn oil vehicle alone, daily for 10 weeks via gastric gavage. The rats' oestrous cycle was consistently evaluated from the initiation of BPA exposure, and observation was continued for 21 days after the exposure had ended. Serum sex hormone concentrations, blood glucose metabolism, ovarian morphology and fertility were investigated. Results: Adolescent exposure to BPA resulted in irregular oestrous cycles and abnormal ovulation in female rats. Compared with the control group, BPA exposure increased the serum concentrations of testosterone, LH, insulin and glucagon, but reduced the serum

concentrations of oestradiol, prolactin, sex hormone-binding globulin and anti-Mullerian hormone. BPA exposure during adolescence caused ovarian atrophy in the rats in adulthood but did not lead to polycystic changes in the ovaries. Moreover, female rats exposed to BPA showed a significant decrease in terms of litter number and weight. Conclusions: Exposure of adolescent female rats to BPA induced a PCOS-like syndrome that was similar to clinical subtype B of PCOS in adulthood and led to a marked decline in fertility. The findings further extend the research on endocrine-disrupting chemicals in reproduction, which would help to shed light on the pathogenesis of PCOS.
https://doi.org/10.1016/j.rbmo.2025.104831