Bulletin de veille Perturbateurs Endocriniens N°24 - mars / avril 2024

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

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

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

Exposition professionnelle

Adult Organophosphate and Carbamate Insecticide Exposure and Sperm Concentration: A Systematic Review and Meta-Analysis of the Epidemiological Evidence,

ELLIS L. B., K. MOLINA, C. R. ROBBINS, M. FREISTHLER, D. SGARGI, D. MANDRIOLI and M. J. PERRY,

Environmental Health Perspectives 131, no. 11 (Nov 2023),

Evidence of the negative impacts of contemporary use insecticides on sperm concentration has increased over the last few decades; however, meta-analyses on this topic are rare. This

investigation assessed the qualitative and quantitative strength of epidemiological evidence regarding adult exposure to two classes of contemporary use insecticides—organophosphates (OPs) and -methyl carbamates (NMCs)—and sperm concentration using robust and reproducible systematic review and meta-analysis methods. Three scientific databases (PubMed, Scopus, and Web of Science), two U.S. government databases (NIOSHTIC-2 and Science.gov), and five nongovernmental organization websites were searched for relevant primary epidemiological studies published in any language through 11 August 2022. Risk of bias and strength of evidence were evaluated according to Navigation Guide systematic review methodology. Bias-adjusted standardized mean difference effect sizes were calculated and pooled using a three-level, multivariate random-effect meta-analysis model with cluster-robust variance estimation. Across 20 studies, 21 study populations, 42 effect sizes, and 1,774 adult men, the pooled bias-adjusted standardized mean difference in sperm concentration between adult men more- and less-exposed to OP and NMC insecticides was (95% CI: , ;). Sensitivity and subgroup analyses explored statistical heterogeneity and validated the model robustness. Although the pooled effect estimate was modified by risk of bias, insecticide class, exposure setting, and recruitment setting, it remained negative in direction across all meta-analyses. The body of evidence was rated to be of moderate quality, with sufficient evidence of an association between higher adult OP and NMC insecticide exposure and lower sperm concentration. This comprehensive investigation found sufficient evidence of an association between higher OP and NMC insecticide exposure and lower sperm concentration in adults. Although additional cohort studies can be beneficial to fill data gaps, the strength of evidence warrants reducing exposure to OP and NMC insecticides now to prevent continued male reproductive harm.

https://doi.org/10.1289/ehp12678

Association between job control and time to pregnancy in a preconception cohort,

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Fertility and Sterility 121, no. 3 (Mar 2024): 497-505,

Objective: To evaluate associations between low job control (operationalized as job independence and freedom to make decisions) and time to pregnancy. Low job control, a form of workplace stress, is associated with adverse health outcomes ranging from cardiovascular disease to premature mortality; few studies have specifically examined its association with reproductive outcomes. Design: We used data from Pregnancy Study Online, an internet-based preconception cohort study of couples trying to conceive in the United States and Canada. We estimated fecundability ratios (FRs) and 95% confidence intervals (CIs) via proportional probability regression models, adjusting for sociodemographic and behavioral characteristics. Setting: Not applicable (Web -based study). Patients: Participants self -identified as female, were aged 21-45 years, and reported %6 cycles of pregnancy attempt time at enrollment (2018-2022). Exposure: We assessed job control by matching participants' baseline self -reported occupation and industry with standardized occupation codes from the National Institute for Occupational Safety and Health's Industry and Occupation Computerized Coding System, then linking codes to O*NET job exposure scores for job independence and freedom to make decisions. Main Outcome Measure: Our main outcome measure was fecundability. Participants completed self-administered questionnaires at baseline and every 8 weeks for up to 12 months or until reported pregnancy, whichever occurred first. Results: Among 3,110 participants, lower job independence was associated with reduced fecundability. Compared with the fourth (highest) quartile, corresponding to the most job independence, FRs (95% CI) for first (lowest), second, and third quartiles were 0.92 (0.82-1.04), 0.84

(0.74-0.95), and 0.99 (0.88, 1.11), respectively. Lower freedom to make decisions was associated with slightly reduced fecundability (first vs. fourth quartile: FR 1/4 0.92; 95% CI: 0.80-1.05). Conclusion: Lower job control, a work -related stressor, may adversely influence time to pregnancy. Because job control is a condition of work (i.e., not modifiable by individuals), these findings may strengthen arguments for improving working conditions as a means of improving worker health, including fertility. (Fertil Sterile 2024;121:497-505. (c) 2023 by American Society for Reproductive Medicine.) El resumen esta disponible en Espanol al final del articulo. https://doi.org/10.1016/j.fertnstert.2023.11.022

Firefighting, per- and polyfluoroalkyl substances, and DNA methylation of genes associated with prostate cancer risk,

QUAID M., J. M. GOODRICH, M. M. CALKINS, J. M. GRABER, D. URWIN, J. GABRIEL, A. J. CABAN-MARTINEZ, R. L. PETROFF, C. GRANT, S. C. BEITEL, S. LITTAU, J. J. GULOTTA, D. WALLENTINE, J. HUGHES and J. L. BURGESS,

Environmental and Molecular Mutagenesis 65, no. 1-2 (Jan 2024): 55-66,

Prostate cancer is the leading incident cancer among men in the United States. Firefighters are diagnosed with this disease at a rate 1.21 times higher than the average population. This increased risk may result from occupational exposures to many toxicants, including per- and polyfluoroalkyl substances (PFAS). This study assessed the association between firefighting as an occupation in general or PFAS serum levels, with DNA methylation. Only genomic regions previously linked to prostate cancer risk were selected for analysis: GSTP1, Alu repetitive elements, and the 8q24 chromosomal region. There were 444 male firefighters included in this study, with some analyses being conducted on fewer participants due to missingness. Statistical models were used to test associations between exposures and DNA methylation at CpG sites in the selected genomic regions. Exposure variables included proxies of cumulative firefighting exposures (incumbent versus academy status and years of firefighting experience) and biomarkers of PFAS exposures (serum concentrations of 9 PFAS). Proxies of cumulative exposures were associated with DNA methylation at 15 CpG sites and one region located within FAM83A (q-value <0.1). SbPFOA was associated with 19 CpG sites ($q < 0.1$), but due to low detection rates, this PFAS was modeled as detected versus not detected in serum. Overall, there is evidence that firefighting experience is associated with differential DNA methylation in prostate cancer risk loci, but this study did not find evidence that these differences are due to PFAS exposures specifically. https://doi.org/10.1002/em.22589

Pesticide use patterns and their association with cytokine levels in Mexican flower workers,

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International Archives of Occupational and Environmental Health 97, no. 3 (2024/04/01 2024): 291-302,

Occupational exposure to pesticides is a known risk for disrupting cellular immune response in flower workers due to their use of multiple chemical products, poor work conditions, and inadequate protection. Recently, the analysis of pesticide use patterns has emerged as an alternative to studying exposure to mixtures of these products. This study aimed to evaluate the association between exposure to different patterns of pesticide use and the cytokine profile of flower workers in the State of Mexico and Morelos, Mexico. https://doi.org/10.1007/s00420-023-02043-x

Epidémiologie

Association between mixed exposure to endocrine-disrupting chemicals and cognitive function in elderly Americans,

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Public Health 228 (Mar 2024): 36-42,

Objectives: Studies exploring the relationship between mixed exposure to endocrine-disrupting chemicals (EDCs) and cognition are limited, with even more scarce studies conducted in the elderly. The aim of this study was to investigate the association between mixed exposure to five categories of EDCs and cognition in elderly Americans. Study design: Cross-sectional study. Methods: 727 participants from the 2011-2014 National Health and Nutrition Examination Survey were incorporated into this study, and the levels of 47 EDC metabolites were measured. Cognitive function was assessed using immediate recall test (IRT), delayed recall test (DRT), animal fluency test (AFT), and digit symbol substitution test (DSST), and all the cognitive test scores were standardized. The individual and combined effects of EDC metabolites on the cognitive function in older adults were assessed using three analytical methods. Results: The results showed that exposure to perfluorononanoic acid, polychlorinated biphenyl (PCB) 199, and PCB 206 was associated with the z-scores on the cognitive tests. Negative associations between mixed exposure to EDCs and the AFT and Global z-scores and a positive relationship with the DRT z-score were found in the WQS regression. The BKMR results revealed a positive trend between the mixture of EDCs and the DRT z-score. However, compared to the median, exposure to mixtures in the 45th percentile and below was associated with a decreased DRT z-score. Conclusions: Mixed exposure to EDCs may adversely affect the global cognitive function in elderly individuals. Necessary measures are needed to restrict EDCs use to protect the cognitive health of older adults.
https://doi.org/10.1016/j.puhe.2023.12.021

Association between per- and polyfluoroalkyl substances exposure and thyroid function biomarkers among females attending a fertility clinic,

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Environmental Pollution 346 (Apr 2024),

Per- and polyfluoroalkyl substances (PFAS) exposure was associated with changes in thyroid function in pregnant mothers and the general population. Limited such evidence exists in other susceptible populations such as females with fertility problems. This cross-sectional study included 287 females seeking medically assisted reproduction at a fertility clinic in Massachusetts, United States, between 2005 and 2019. Six long-alkyl chain PFAS, thyroid hormones, and autoimmune antibodies were quantified in baseline serum samples. We used generalized linear models and quantile g-computation to evaluate associations of individual PFAS and their total mixture with thyroid biomarkers. Most females were White individuals (82.7%), had graduate degrees (57.8%), and nearly half had unexplained subfertility (45.9%). Serum concentrations of all examined PFAS

and their mixture were significantly associated with 2.6%-5.6% lower total triiodothyronine (TT3) concentrations. Serum concentrations of perfluorononanoate (PFNA), perfluorodecanoate (PFDA), and perfluoroundecanoate (PFUnDA), and of the total mixture were associated with higher ratios of free thyroxine (FT4) to free triiodothyronine (FT3). No associations were found for PFAS and TSH or autoimmune antibodies. Our findings support the thyroid-disrupting effect of long alkyl-chain PFAS among a vulnerable population of subfertile females.
https://doi.org/10.1016/j.envpol.2024.123513

The association between prenatal exposure to bisphenol A and offspring obesity: A systematic review,

GUO J. J., K. Q. LIU, J. X. YANG and Y. W. SU,

Environmental Pollution 344 (Mar 2024),

In recent years, the global prevalence of childhood overweight and obesity has surged. Bisphenol A (BPA), prevalent in the manufacture of polycarbonate plastics and epoxy resins, is associated with this escalating obesity pattern. Both early life stages and pregnancy emerge as pivotal windows of vulnerability. This review systematically evaluates human studies to clarify the nexus between prenatal BPA exposure and offspring obesity. Our extensive literature search covered databases like PubMed, Web of Science, Cochrane Library, Embase, and Scopus, encompassing articles from their inception until July 2023. We utilized the Newcastle-Ottawa Scale (NOS) to evaluate the methodological rigor of the included studies, the Oxford Center for Evidence-Based Medicine Levels of Evidence Working Group (OCEBM) table to determine the level of the evidence, and the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) guidelines to evaluate the certainty of the evidence with statistical significance. We centered on primary studies investigating the link between urinary BPA levels during pregnancy and offspring obesity. Our analysis included thirteen studies, with participant counts ranging from 173 to 1124 mother-child dyads. Among them, eight studies conclusively linked prenatal BPA exposure to increased obesity in offspring. Evaluation metrics for the effect of prenatal BPA on offspring obesity comprised BMI z-score, waist circumference, overweight/obesity classification, aggregate skinfold thickness, body fat percentage, and more. Present findings indicate that prenatal BPA exposure amplifies offspring obesity risk, with potential effect variations by age and gender. Therefore, further research is needed to explore the causal link between prenatal BPA exposure and obesity at different developmental stages and genders, and to elucidate the underlying mechanisms.
https://doi.org/10.1016/j.envpol.2024.123391

Association of maternal exposure to endocrine disruptor chemicals with cardio-metabolic risk factors in children during childhood: a systematic review and meta-analysis of cohort studies,

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Diabetology & Metabolic Syndrome 16, no. 1 (Apr 2024),

Background In the present systematic review and meta-analysis, the association of maternal exposure to the endocrine disrupting chemicals (EDCs) with cardio-metabolic risk factors in children during childhood for the first time. Method The PubMed, Scopus, EMBASE, and Web of Science databases were systematically searched, up to Feb 2023. In total 30 cohort studies had our inclusion criteria. A random-effects model was used for the variables that had considerable heterogeneity between studies. The Newcastle-Ottawa Scale (NOS) tool was used to classify the

quality score of studies. All statistical analyses were conducted using Stata 14 and P-value < 0.05 considered as a significant level. Results In the meta-analysis, maternal exposure to the EDCs was weakly associated with higher SBP (Fisher_Z: 0.06, CI: 0.04, 0.08), BMI (Fisher_Z: 0.07, CI: 0.06, 0.08), and WC (Fisher_Z: 0.06, CI: 0.03, 0.08) z-scores in children. A significant linear association was found between maternal exposure to the bisphenol-A and pesticides with BMI and WC z-score in children ($p < 0.001$). Subgroup analysis showed significant linear association of BPA and pesticides, in the urine samples of mothers at the first trimester of pregnancy, with BMI and WC z-score in children from 2-8 years ($p < 0.05$). Conclusion Prenatal exposure to the EDCs in the uterine period could increase the risk of obesity in children. Maternal exposure to bisphenol-A and pesticides showed the strongest association with the obesity, especially visceral form, in the next generation. https://doi.org/10.1186/s13098-024-01320-0

Association of maternal phthalates exposure and metabolic gene polymorphisms with congenital heart diseases: a multicenter case-control study,

LI N. N., H. KANG, Z. LIU, L. LI, Y. DENG, M. X. WANG, Y. T. LI, W. L. XU, X. H. LI, Y. P. WANG, J. ZHU, J. TAO and P. YU,

Bmc Pregnancy and Childbirth 24, no. 1 (Feb 2024),

BackgroundThe majority of congenital heart diseases (CHDs) are thought to result from the interactions of genetics and the environment factors. This study aimed to assess the association of maternal non-occupational phthalates exposure, metabolic gene polymorphisms and their interactions with risk of CHDs in offspring.MethodsA multicenter case-control study of 245 mothers with CHDs infants and 268 control mothers of health infant was conducted from six hospitals. Maternal urinary concentrations of eight phthalate metabolites were measured by ultra-high performance liquid chromatography coupled with tandem mass spectrometry (UHPLC-MS/MS). Twenty single nucleotide polymorphisms (SNPs) in cytochrome P450 family 2 subfamily C member 9 (CYP2C9) and 19 (CYP2C19), uridine diphosphate (UDP) glucuronosyl transferase family 1 member A7 (UGT1A7), family 2 member B7 (UGT2B7) and B15(UGT2B15) genes were genotyped. The multivariate logistic regressions were used to estimate the association between maternal phthalates exposure or gene polymorphisms and risk of CHDs. Generalized multifactor dimensionality reduction (GMDR) was used to analyze the gene-gene and gene-phthalates exposure interactions.ResultsThere was no significant difference in phthalate metabolites concentrations between the cases and controls. No significant positive associations were observed between maternal exposure to phthalates and CHDs. The SNPs of UGT1A7 gene at rs4124874 (under three models, log-additive: aOR = 1.74, 95% CI:1.28-2.37; dominant: aOR = 1.86, 95% CI:1.25-2.78; recessive: aOR = 2.50, 95% CI: 1.26-4.94) and rs887829 (under the recessive model: aOR = 13.66, 95% CI: 1.54-121) were significantly associated with an increased risk of CHDs. Furthermore, the associations between rs4124874 (under log-additive and dominant models) of UGT1A7 were statistically significant after the false discovery rate correction. No significant gene-gene or gene-phthalate metabolites interactions were observed.ConclusionsThe polymorphisms of maternal UGT1A7 gene at rs4124874 and rs887829 were significantly associated with an increased risk of CHDs. More large-scale studies or prospective study designs are needed to confirm or refute our findings in the future. https://doi.org/10.1186/s12884-024-06343-z

Associations of parental preconception and maternal pregnancy urinary phthalate biomarker and bisphenol-a concentrations with child eating behaviors,

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International Journal of Hygiene and Environmental Health 257 (Apr 2024),

Background: Eating behaviors are controlled by the neuroendocrine system. Whether endocrine disrupting chemicals have the potential to affect eating behaviors has not been widely studied in humans. We investigated whether maternal and paternal preconception and maternal pregnancy urinary phthalate biomarker and bisphenol-A (BPA) concentrations were associated with children's eating behaviors. Methods: We used data from mother -father -child triads in the Preconception Environmental exposure And Childhood health Effects (PEACE) Study, an ongoing prospective cohort study of children aged 6-13 years whose parent(s) previously enrolled in a fertility clinic -based prospective preconception study. We quantified urinary concentrations of 11 phthalate metabolites and BPA in parents' urine samples collected preconceptionally and during pregnancy. Parents rated children's eating behavior using the Child Eating Behavior Questionnaire (CEBQ). Using multivariable linear regression, accounting for correlation among twins, we estimated covariateadjusted associations of urinary phthalate biomarkers and BPA concentrations with CEBQ subscale scores. Results: This analysis included 195 children (30 sets of twins), 160 mothers and 97 fathers; children were predominantly non -Hispanic white (84%) and 53% were male. Paternal and maternal preconception monobenzyl phthalate (MBzP) concentrations and maternal preconception mono -n -butyl phthalate (MnBP) were positively associated with emotional overeating, food responsiveness, and desire to drink scores in children (beta ' s = 0.11 [95% CI: 0.01, 0.20]-0.21 [95% CI: 0.10, 0.31] per loge unit increase in phthalate biomarker concentration). Paternal preconception BPA concentrations were inversely associated with scores on food approaching scales. Maternal pregnancy MnBP, mono-isobutyl phthalate (MiBP) and MBzP concentrations were associated with increased emotional undereating scores. Maternal pregnancy monocarboxy-isononyl phthalate concentrations were related to decreased food avoiding subscale scores. Conclusions: In this cohort, higher maternal and paternal preconception urinary concentrations of some phthalate biomarkers were associated with increased food approaching behavior scores and decreased food avoiding behavior scores, which could lead to increased adiposity in children.
https://doi.org/10.1016/j.ijheh.2024.114334

Associations of pyrethroid exposure with bone mineral density and osteopenia in adults,

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Journal of Bone and Mineral Metabolism 42, no. 2 (Mar 2024): 242-252,

Introduction This study was to investigate the correlations between pyrethroid exposure and bone mineral density (BMD) and osteopenia. Materials and methods This cross-sectional study included 1389 participants over 50 years of age drawn from the 2007-2010 and 2013-2014 National Health and Nutrition Examination Survey (NHANES). Three pyrethroid metabolites, 3-phenoxybenzoic acid (3-PBA), trans-3-(2,2-dichlorovinyl)-2,2-dimethyl-cyclopropane-1-carboxylic acid (trans-DCCA), and 4-fluoro-3-phenoxybenzoic acid (4-F-3PBA) were used as indicators of pyrethroid exposure. Low BMD was defined as T-score < - 1.0, including osteopenia. Weighted multivariable linear regression analysis or logistic regression analysis was utilized to evaluate the correlation between pyrethroid exposure and BMD and low BMD. Bayesian kernel machine regression (BKMR) model was utilized to analyze the correlation between pyrethroids mixed exposure and low BMD. Results There were 648 (48.41%) patients with low BMD. In individual pyrethroid metabolite analysis, both tertile 2 and tertile 3 of trans-DCCA were negatively related to total femur, femur neck, and total spine BMD

[coefficient (beta) = - 0.041 to - 0.028; all P < 0.05]. Both tertile 2 and tertile 3 of 4-F-3PBA were negatively related to total femur BMD (P < 0.05). Only tertile 2 [odds ratio (OR) = 1.63; 95% CI = 1.07, 2.48] and tertile 3 (OR = 1.65; 95% CI = 1.10, 2.50) of trans-DCCA was correlated with an increased risk of low BMD. The BKMR analysis indicated that there was a positive tendency between mixed pyrethroids exposure and low BMD. Conclusion In conclusion, pyrethroids exposure was negatively correlated with BMD levels, and the associations of pyrethroids with BMD and low BMD varied by specific pyrethroids, pyrethroid concentrations, and bone sites. https://doi.org/10.1007/s00774-024-01499-2

A comprehensive multiplatform metabolomic analysis reveals alterations of 2-hydroxybutyric acid among women with deep endometriosis related to the pesticide trans-nonachlor,

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Science of the Total Environment 918 (Mar 2024),

Background: Exposure to persistent organic pollutants (POPs) has been related to the risk of endometriosis however the mechanisms remain unclear. The objective of the present study was to characterize the metabolic profiles underpinning the associations between POPs and endometriosis risk. Methodology: A hospital-based case-control study was conducted in France to recruit women with and without surgically confirmed deep endometriosis. Women's serum was analyzed using gas and liquid chromatography coupled to high -resolution mass spectrometry (HRMS) to measure the levels of polychlorinated biphenyls (PCBs), organochlorinated pesticides (OCPs) and per-/polyfluoroalkyl substances (PFAS). A comprehensive metabolomic profiling was conducted using targeted HRMS and 1H nuclear magnetic resonance (1H NMR) to cover polar and non -polar fractions. A "meet -in -the -middle" statistical framework was applied to identify the metabolites related to endometriosis and POP levels, using multivariate linear and logistic regressions adjusting for confounding variables. Results: Fourteen PCBs, six OCPs and six PFAS were widely found in almost all serum samples. The pesticide trans-nonachlor was the POP most strongly and positively associated with deep endometriosis risk, with odds ratio (95 % confidence interval) of 2.42 (1.49; 4.12), followed by PCB180 and 167. Women with endometriosis exhibited a distinctive metabolic profile, with elevated serum levels of lactate, ketone bodies and multiple amino acids and lower levels of bile acids, phosphatidylcholines (PCs), cortisol and hippuric acid. The metabolite 2hydroxybutyrate was simultaneously associated to endometriosis risk and exposure to trans-nonachlor. Conclusions: To the best of our knowledge, this is the first comprehensive metabolome-wide association study of endometriosis, integrating ultra -trace profiling of POPs. The results confirmed a metabolic alteration among women with deep endometriosis that could be also associated to the exposure to POPs. Further observational and experimental studies will be required to delineate the causal ordering of those associations and gain insight on the underlying mechanisms. https://doi.org/10.1016/j.scitotenv.2024.170678

Dietary intakes of dioxins and polychlorobiphenyls (PCBs) and mortality: EPIC cohort study in 9 European countries,

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International Journal of Hygiene and Environmental Health 255 (Jan 2024),

Dioxins and polychlorinated biphenyls (PCBs) are toxic, endocrine disruptors and persistent chemicals for which the main exposure source is diet due to their bioaccumulation and biomagnification in food chains. Cohort studies in the general populations have reported inconsistent associations between these chemicals in serum/plasma and mortality. Our objective was to study the association between dietary intake of 17 dioxins and 35 PCBs and all-cause, cancer-specific and cardiovascular-specific mortalities were assessed in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Dietary intake of dioxins and PCBs was assessed combining EPIC food consumption data with European food contamination data provided by the European Food Safety Authority. We applied multivariable Cox regressions. The analysis included 451,390 adults (mean +/- SD age:51.1 +/- 9.7 years) with 46,627 deaths and a median follow-up of 17.4 years (IQR = 15.2-19.1). A U-shaped non-linear association with all-cause mortality for dietary intake of dioxins (Pnon-linearity<0.0001), DL-PCB (Pnon-linearity = 0.0001), and NDL-PCBs (Pnon-linearity<0.01) was observed. For example, the hazard ratios (95%Confidance interval) for all-cause mortality obtained with the spline model was equal to 1.03 (1.02-1.05) for low levels of intake to dioxins (7 pg TEQ/day), 0.93 (0.90-0.96) for moderate levels of intake (25 pg TEQ/day), while for high levels of intake (55 pg TEQ/day) it was 1.03 (0.97-1.09). Intake of dioxins, DL-PCBs and NDL-PCBs was not associated with cardiovascular mortality. There was no association between intakes of dioxins and cancer mortality, but a U-shaped association was observed for intake of DL-PCBs and intakes of NDL-PCBs and cancer mortality. The PCBs and dioxins are known to have endocrine disrupting properties which can lead to non-monotonic dose responses. These results need to be interpreted with caution and further studies are needed to better clarify the association between dietary intake of dioxins and PCB and mortality in the general population. https://doi.org/10.1016/j.ijheh.2023.114287

Does Bisphenol-A play a role in the development of neural tube defects?,

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Journal of Perinatology (2024 Mar 2024),

ObjectiveIn this study, we aimed to evaluate BPA levels in the maternal serum and amniotic fluid of patients diagnosed with NTD. In addition, we wanted to investigate the relationship between neurodevelopmental defects, such as neural tube defects (NTD), and BPA levels.Study designThis prospective observational study was carried out at Bursa Yuksek Ihtisas Training and Research Hospital between April 15, 2021, and April 15, 2022. The study consisted of 92 patients between the ages of 18-45 who had an amniocentesis at 15-22 weeks of gestation. The patients were divided into two groups according to the indications of amniocentesis. Group 1 contained the patients with abnormal maternal serum screening results or cell-free DNA results and abnormal ultrasonography findings (45 patients). Group 2 contained the patients with a pre-diagnosis of NTD (47 patients). The first 5 cc fluids and maternal serum samples taken during the amniocentesis procedure of all patients were delivered to the biochemistry laboratory. The BPA values between groups were compared.ResultsA statistically significant difference was found between the two groups in terms of amniotic fluid BPA levels (36.66 (19.00:82.00) and 39.62 (19.02-73.87)) and maternal blood BPA levels (22.26 (12.60-228) and 47.81 (12.89-228.39)). In cases with NTD, amniotic fluid BPA levels and maternal blood BPA levels were significantly higher than the control group. When AUC values were compared, the AFP numerical value was higher than the amniotic fluid and maternal blood BPA levels.ConclusionPlastic, which is indispensable for modern life, may negatively affect fetal development in intrauterine life. The data in this study says that high maternal blood BPA may be associated with NTD. https://doi.org/10.1038/s41372-024-01925-3

EDC mixtures during pregnancy and body fat at 7 years of age in a Swedish cohort, the SELMA study,

SVENSSON K., C. GENNINGS, C. LINDH, H. KIVIRANTA, P. RANTAKOKKO, S. WIKSTRO and C. G. BORNEHAG,

Environmental Research 248 (May 2024),

Background: Some endocrine disrupting chemicals (EDC), are "obesogens" and have been associated with overweight and obesity in children. Daily exposure to different classes of EDCs demands for research with mixtures approach. Objectives: This study evaluates the association, considering sex-specific effects, between prenatal exposure to EDC mixture and children's body fat at seven years of age. Methods: A total of 26 EDCs were assessed in prenatal urine and serum samples from first trimester in pregnancy from 737 mother-child pairs participating in the Swedish Environmental Longitudinal, Mother and child, Asthma and allergy (SELMA) study. An indicator for children's "overall body fat" was calculated, using principal component analysis (PCA), based on BMI, percent body fat, waist, and skinfolds measured at seven years of age. Weighted quantile sum (WQS) regression was used to assess associations between EDC mixture and children's body fat. Results: Principal component (PC1) represented 83.6 % of the variance, suitable as indicator for children's "overall body fat", with positive loadings of 0.40-0.42 for each body fat measure. A significant interaction term, WQS*sex, confirmed associations in the opposite direction for boys and girls. Higher prenatal exposure to EDC mixture was borderline significant with more "overall body fat" for boys (Mean beta = 0.20; 95 % CI: -0.13, 0.53) and less for girls (Mean beta = -0.23; 95 % CI: -0.58, 0.13). Also, higher prenatal exposure to EDC mixture was borderline significant with more percent body fat (standardized score) for boys (Mean beta = 0.09; 95 % CI: -0.04, 0.21) and less for girls (Mean beta = -0.10 (-0.26, 0.05). The chemicals of concern included bisphenols, phthalates, PFAS, PAH, and pesticides with different patterns for boys and girls. Discussion: Borderline significant associations were found between prenatal exposure to a mixture of EDCs and children's body fat. The associations in opposite directions suggests that prenatal exposure to EDCs may present sex-specific effects on children's body fat.
https://doi.org/10.1016/j.envres.2024.118293

Effects of Pharmaceutical Substances with Obesogenic Activity on Male Reproductive Health,

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International Journal of Molecular Sciences 25, no. 4 (Feb 2024),

Obesogens have been identified as a significant factor associated with increasing obesity rates, particularly in developed countries. Substances with obesogenic traits are prevalent in consumer products, including certain pharmaceuticals. Specific classes of pharmaceuticals have been recognized for their ability to induce weight gain, often accompanied by hormonal alterations that can adversely impact male fertility. Indeed, research has supplied evidence underscoring the crucial role of obesogens and therapeutic agents in the normal functioning of the male reproductive system. Notably, sperm count and various semen parameters have been closely linked to a range of environmental and nutritional factors, including chemicals and pharmacological agents exhibiting obesogenic properties. This review aimed to explore studies focused on analyzing male fertility parameters, delving into the intricacies of sperm quality, and elucidating the direct and adverse effects that pharmacological agents may have on these aspects.
https://doi.org/10.3390/ijms25042324

Exploring autism spectrum disorder (ASD) and attention deficit disorder (ADD/ADHD) in children exposed to polybrominated biphenyl,

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Environmental Epidemiology 8, no. 2 (Apr 2024),

Background:Although the causes of attention-deficit/hyperactivity disorder (ADHD) and autism have not been identified, exposure to endocrine-disrupting chemicals, such as polybrominated biphenyl (PBB), during fetal development and early life has been suspected to impact neurological development. This study aims to investigate the association between prenatal and early life exposure to PBB and the development of ADHD and autism later in life.Methods:Data from the Michigan PBB Registry, a cohort of Michigan residents who had been exposed to PBB in a mass contamination event in 1973, was leveraged for this nested case-control analysis among two distinct samples: (1) Those who self-reported ADHD or autism diagnosis, and (2) mothers who reported their child's ADHD or autism diagnosis. PBB exposure was measured in participants of the PBB Registry, and the mother's PBB level was used in mother-reported analyses. Cases were matched with controls by sex and year of birth. Conditional logistic regression models were used to estimate the association between PBB level and case status.Results:PBB levels were higher among those who were exposed in early life compared with those exposed in utero (geometric mean: 0.300 ng/ml vs. 0.016 ng/ml). Among women in this cohort, a higher than expected proportion of self-reported ADHD diagnosis (11.11%), compared with population estimates. PBB was not associated with ADHD or autism in either self-reported or mother-reported analyses.Conclusions:This study adds to the sparse literature about prenatal and early life exposure to PBB-153 and ADHD and autism. Future studies should examine potential effect modification by sex. https://doi.org/10.1097/ee9.0000000000000304

Exposure to Endocrine-Disrupting Chemicals and Congenital Heart Diseases: The Pooled Results Based on the Current Evidence,

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Pediatric Cardiology (2024 Apr 2024),

The relationships between maternal exposure to endocrine-disrupting chemicals (EDCs) and congenital heart diseases (CHD) are not elucidated yet. The exposure levels of EDCs are generally estimated based on self-reported questionnaires or occupational exposure evaluations in the literature. Therefore, a study based on epidemiological data from human biospecimens is required to provide stronger evidence between maternal exposure to EDC and CHD. Embase, Pubmed, Scopus, and the Cochrane Library databases were searched for related research which provided risk estimates regarding the relationships between maternal EDC exposure and CHD in human offspring. Baseline characteristics and outcomes of CHD were extracted from each included study. Odds ratios (ORs) with 95% confidence intervals (CIs) were pooled to calculate the overall estimates of CHD. Subgroup and meta-regression analyses were performed to identify the sources of heterogeneity. Bootstrapping techniques were used in analyses where several studies originated from a similar population. A total of seventeen studies were involved in the meta-analyses. Maternal EDC exposure was significantly related to CHD in offspring (OR 2.15; 95%CI 1.64 to 2.83). EDC exposure was significantly associated with septal defects (OR 2.34; 95%CI 1.77 to 3.10), conotruncal defects (OR 2.54; 95%CI 1.89 to 3.43), right ventricular outflow tract obstruction (OR

2.65; 95%CI 1.73 to 4.07), left ventricular outflow tract obstruction (OR 3.58; 95%CI 2.67 to 4.79), anomalous pulmonary venous return (OR 2.31; 95%CI 1.34 to 4.00), and other heart defects (OR 2.49; 95%CI 1.75 to 3.54). In addition, maternal exposure to heavy metals, which included lead (OR 2.19; 95%CI 1.29 to 3.71), cadmium (OR 1.81; 95%CI 1.28 to 2.56), mercury (OR 2.23; 95%CI 1.13 to 4.44), and manganese (OR 2.65; 95%CI 1.48 to 4.74), increased risks for CHD significantly. In conclusion, based on the latest evidence, maternal EDC exposure may increase CHD risks in human offspring, especially in heavy metal exposure conditions. https://doi.org/10.1007/s00246-024-03478-w

Exposure to Short- and Medium-Chain Chlorinated Paraffins and the Risk of Gestational Diabetes Mellitus: A Nested Case-Control Study in Eastern China,

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Environmental Science & Technology 58, no. 8 (Feb 2024): 3665-3676,

Toxicological studies have indicated that exposure to chlorinated paraffins (CPs) may disrupt intracellular glucose and energy metabolism. However, limited information exists regarding the impact of human CP exposure on glucose homeostasis and its potential association with an increased risk of developing gestational diabetes mellitus (GDM). Here, we conducted a prospective study with a nested case-control design to evaluate the link between short- and medium-chain CP (SCCPs and MCCPs) exposures during pregnancy and the risk of GDM. Serum samples from 102 GDM-diagnosed pregnant women and 204 healthy controls were collected in Hangzhou, Eastern China. The median (interquartile range, IQR) concentration of SCCPs was 161 (127, 236) ng/mL in the GDM group compared to 127 (96.9, 176) ng/mL in the non-GDM group ($p < 0.01$). For MCCPs, the GDM group had a median concentration of 144 (117, 174) ng/mL, while the control group was 114 (78.1, 162) ng/mL ($p < 0.01$). Compared to the lowest quartile as the reference, the adjusted odds ratios (ORs) of GDM were 7.07 (95% CI: 2.87, 17.40) and 3.34 (95% CI: 1.48, 7.53) in the highest quartile of n-ary sumation SCCP and n-ary sumation MCCP levels, respectively, with MCCPs demonstrating an inverted U-shaped association with GDM. Weighted quantile sum regression evaluated the joint effects of all CPs on GDM and glucose homeostasis. Among all CP congeners, $C_{13}H_{23}Cl_5$ and $C_{10}H_{16}Cl_6$ were the crucial variables driving the positive association with the GDM risk. Our results demonstrated a significant positive association between CP concentration in maternal serum and GDM risk, and exposure to SCCPs and MCCPs may disturb maternal glucose homeostasis. These findings contribute to a better understanding of the health risks of CP exposure and the role of environmental contaminants in the pathogenesis of GDM.
https://doi.org/10.1021/acs.est.3c08064

Influence of maternal endocrine disrupting chemicals exposure on adverse pregnancy outcomes: A systematic review and meta-analysis,

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Ecotoxicology and Environmental Safety 270 (Jan 2024),

Maternal endocrine disrupting chemicals (EDCs) exposure, the common environmental pollutants, was capable of involving in adverse pregnancy outcomes. However, the evidence of their connection is not consistent. Our goal was to comprehensively explore the risk of EDCs related to adverse pregnancy outcomes. One hundred and one studies were included from two databases

before 2023 to explore the association between EDCs and adverse pregnancy outcomes including miscarriage, small for gestational age (SGA), low birth weight (LBW) and preterm birth (PTB). We found that maternal PFASs exposure was positively correlated with PTB (OR:1.13, 95% CI:1.04-1.23), SGA (OR:1.10, 95% CI:1.04-1.16) and miscarriage (OR:1.09, 95% CI:1.00-1.19). The pooled estimates also showed maternal PAEs exposure was linked with PTB (OR:1.16, 95% CI:1.11-1.21), SGA (OR:1.20, 95% CI:1.07-1.35) and miscarriage (OR:1.55, 95% CI:1.33-1.81). In addition, maternal exposure to some specific class of EDCs including PFOS, MBP, MEHP, DEHP, and BPA was associated with PTB. Maternal exposure to PFOS, PFOA, PFHpA was associated with SGA. Maternal exposure to BPA was associated with LBW. Maternal exposure to MMP, MEHP, MEHHP, MEOHP, BPA was associated with miscarriage. Maternal PFASs, PAEs and BPA exposure may increase adverse pregnancy outcomes risk according to our study. However, the limited number of studies on dose-response hampered further explanation for causal association.
https://doi.org/10.1016/j.ecoenv.2023.115851

Long-term exposure to ambient PM_{2.5} and its components on menarche timing among Chinese adolescents: evidence from a representative nationwide cohort,

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Bmc Public Health 24, no. 1 (Mar 2024),

Background Ambient air pollutants have been suggested to affect pubertal development. Nevertheless, current studies indicate inconsistent effects of these pollutants, causing precocious or delayed puberty onset. This study aimed to explore the associations between long-term exposure to particulate matter with aerodynamic diameters <= 2.5 mu m (PM2.5) along with its components and menarche timing among Chinese girls. Method Self-reported age at menarche was collected among 855 girls from China Health and Nutrition Survey 2004 to 2015. The pre-menarche annual average concentrations of PM2.5 and its components were calculated on the basis of a long-term (2000-2014) high-resolution PM2.5 components dataset. Generalized linear models (GLM) and logistic regression models were used to analyze the associations of exposure to a single pollutant (PM2.5, sulfate, nitrate, ammonium, black carbon and organic matter) with age at menarche and early menarche (< 12 years), respectively. Weighted quantile sum methods were applied to examine the impacts of joint exposure on menarche timing. Results In the adjusted GLM, per 1 mu g/m3 increase of annual average concentrations of nitrate and ammonium decreased age at menarche by 0.098 years and 0.127 years, respectively (all P < 0.05). Every 1 mu g/m3 increase of annual average concentrations of PM2.5 (OR: 1.04, 95% CI: 1.00-1.08), sulfate (OR: 1.23, 95% CI: 1.01-1.50), nitrate (OR: 1.23, 95% CI: 1.06-1.43) and ammonium (OR: 1.32, 95% CI: 1.06-1.66) were significantly positively associated with early menarche. Higher level of joint exposure to PM2.5 and its components was associated with 11% higher odds of early menarche (P = 0.04). Additionally, the estimated weight of sulfate was the largest among the mixed pollutants. Conclusions Long-term exposure to PM2.5 and its components could increase the risk of early menarche among Chinese girls. Moreover, sulfate might be the most critical components responsible for this relationship. Our study provides foundation for targeted prevention of PM2.5 components.
https://doi.org/10.1186/s12889-024-18209-2

Long-term impacts of endocrine-disrupting chemicals exposure on kidney function: A community-based cohort study,

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Environmental Toxicology and Pharmacology 106 (Mar 2024),

This study explores the extended renal effects of endocrine-disrupting chemicals (EDCs) exposure, a linkage already established with adverse health outcomes, notably chronic kidney disease. To delve deeper, the Chang Gung Community Research Center conducted a longitudinal study with 887 participants. Among them, 120 individuals were scrutinized based on EDC scores, analyzing 17 urinary EDCs and renal function. Findings revealed elevated mono-(2-ethylhexyl) phthalate (MEHP) and bisphenol A levels in higher EDC exposure cases. MEHP notably correlated with increased urinary albumin-to-creatinine ratio (UACR), predicting a > 15% decline in estimated glomerular filtration rate. Higher MEHP levels also hinted at declining renal function. UACR escalation linked significantly with specific EDCs: MEHP, methylparaben, nonylphenol, and 4-tert-octylphenol. This research underscores enduring renal hazards tied to environmental EDC exposure, particularly MEHP, emphasizing the urgent call for robust preventive public health strategies.
https://doi.org/10.1016/j.etap.2024.104379

Prenatal phthalate exposure and adverse birth outcomes in the USA: a prospective analysis of births and estimates of attributable burden and costs,

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Lancet Planetary Health 8, no. 2 (Feb 2024),

Background Phthalates are synthetic chemicals widely used in consumer products and have been identified to contribute to preterm birth. Existing studies have methodological limitations and potential effects of di-2-ethylhexyl phthalate (DEHP) replacements are poorly characterised. Attributable fractions and costs have not been quantified, limiting the ability to weigh trade-offs involved in ongoing use. We aimed to leverage a large, diverse US cohort to study associations of phthalate metabolites with birthweight and gestational age, and estimate attributable adverse birth outcomes and associated costs. Methods In this prospective analysis we used extant data in the US National Institutes of Health Environmental influences on Child Health Outcomes (ECHO) Program from 1998 to 2022 to study associations of 20 phthalate metabolites with gestational age at birth, birthweight, birth length, and birthweight for gestational age z-scores. We also estimated attributable adverse birth outcomes and associated costs. Mother-child dyads were included in the study if there were one or more urinary phthalate measurements during the index pregnancy; data on child's gestational age and birthweight; and singleton delivery. Findings We identified 5006 mother-child dyads from 13 cohorts in the ECHO Program. Phthalic acid, diisodecyl phthalate (DiDP), di-n-octyl phthalate (DnOP), and diisononyl phthalate (DiNP) were most strongly associated with gestational age, birth length, and birthweight, especially compared with DEHP or other metabolite groupings. Although DEHP was associated with preterm birth (odds ratio 1 center dot 45 [95% CI 1 center dot 05-2 center dot 01]), the risks per log(10) increase were higher for phthalic acid (2 center dot 71 [1 center dot 91-3 center dot 83]), DiNP (2 center dot 25 [1 center dot 67-3 center dot 00]), DiDP (1 center dot 69 [1 center dot 25-2 center dot 28]), and DnOP (2 center dot 90 [1 center dot 96-4 center dot 23]). We estimated 56 595 (sensitivity analyses 24 003-120 116) phthalate-attributable preterm birth cases in 2018 with associated costs of US$3 center dot 84 billion (sensitivity analysis 1 center dot 63- 8 center dot 14 billion). Interpretation In a large, diverse sample of US births, exposure to DEHP, DiDP, DiNP, and DnOP were associated with decreased gestational age and increased risk of preterm birth, suggesting substantial opportunities for prevention. This finding suggests the adverse consequences of substitution of DEHP with chemically

similar phthalates and need to regulate chemicals with similar properties as a class. https://doi.org/10.1016/S2542-5196(23)00270-X

Toxicité sur l'homme

Advances in understanding the reproductive toxicity of endocrine-disrupting chemicals in women,

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Frontiers in Cell and Developmental Biology 12 (Mar 2024),

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

Assessment of endocrine disruptor impacts on lipid metabolism in a fatty acid-supplemented HepaRG human hepatic cell line,

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Chemosphere 349 (2024/02/01/ 2024): 140883,

The incidence of metabolic dysfunction-associated steatotic liver disease (MASLD) is increasing worldwide. This disease encompasses several stages, from steatosis to steatohepatitis and, eventually, to fibrosis and cirrhosis. Exposure to environmental contaminants is one of the risk factors and an increasing amount of evidence points to a role for endocrine disrupting compounds (EDCs). This study assesses the impact of selected EDCs on the formation of lipid droplets, the marker for steatosis in a hepatic model. The mechanisms underlying this effect are then explored. Ten compounds were selected according to their obesogenic properties: bisphenol A, F and S, butyl-paraben, cadmium chloride, p,p'-DDE, DBP, DEHP, PFOA and PFOS. Using a 2D or 3D model, HepaRG cells were exposed to the compounds with or without fatty acid supplementation. Then, the formation of lipid droplets was quantified by an automated fluorescence-based method. The expression of genes and proteins involved in lipid metabolism and the impact on cellular respiration

was analyzed. The formation of lipid droplets, which is revealed or enhanced by oleic acid supplementation, was most effectively induced by p,p'-DDE and DEHP. Experiments employing either 2D or 3D culture conditions gave similar results. Both compounds induced the expression of PLIN2. p,p'-DDE also appears to act by decreasing in fatty acid oxidation. Some EDCs were able to induce the formation of lipid droplets, in HepaRG cells, an effect which was increased after supplementation of the cells with oleic acid. A full understanding of the mechanisms of these effects will require further investigation. The novel automated detection method described here may also be useful in the future as a regulatory test for EDC risk assessment.
https://doi.org/https://doi.org/10.1016/j.chemosphere.2023.140883

Beyond the Nucleus: Plastic Chemicals Activate G Protein-Coupled Receptors,

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Environmental Science & Technology 58, no. 11 (Mar 2024): 4872-4883,

G protein-coupled receptors (GPCRs) are central mediators of cell signaling and physiological function. Despite their biological significance, GPCRs have not been widely studied in the field of toxicology. Herein, we investigated these receptors as novel targets of plastic chemicals using a high-throughput drug screening assay with 126 human non-olfactory GPCRs. In a first-pass screen, we tested the activity of triphenol phosphate, bisphenol A, and diethyl phthalate, as well as three real-world mixtures of chemicals extracted from plastic food packaging covering all major polymer types. We found 11 GPCR-chemical interactions, of which the chemical mixtures exhibited the most robust activity at adenosine receptor 1 (ADORA1) and melatonin receptor 1 (MTNR1A). We further confirm that polyvinyl chloride and polyurethane products contain ADORA1 or MTNR1 agonists using a confirmatory secondary screen and pharmacological knockdown experiments. Finally, an analysis of the associated gene ontology terms suggests that ADORA1 and MTNR1A activation may be linked to downstream effects on circadian and metabolic processes. This work highlights that signaling disruption caused by plastic chemicals is broader than that previously believed and demonstrates the relevance of nongenomic pathways, which have, thus far, remained unexplored.
https://doi.org/10.1021/acs.est.3c08392

Bisphenol A: Unveiling Its Role in Glioma Progression and Tumor Growth,

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International Journal of Molecular Sciences 25, no. 5 (Mar 2024),

Gliomas represent the most common and lethal category of primary brain tumors. Bisphenol A (BPA), a widely recognized endocrine disruptor, has been implicated in the progression of cancer. Despite its established links to various cancers, the association between BPA and glioma progression remains to be clearly defined. This study aimed to shed light on the impact of BPA on glioma cell proliferation and overall tumor progression. Our results demonstrate that BPA significantly accelerates glioma cell proliferation in a time- and dose-dependent manner. Furthermore, BPA has been found to enhance the invasive and migratory capabilities of glioma cells, potentially promoting epithelial-mesenchymal transition (EMT) characteristics within these tumors. Employing bioinformatics approaches, we devised a risk assessment model to gauge the potential glioma hazards associated with BPA exposure. Our comprehensive analysis revealed that BPA not only facilitates glioma invasion and migration but also inhibits apoptotic processes. In

summary, our study offers valuable insights into the mechanisms by which BPA may promote tumorigenesis in gliomas, contributing to the understanding of its broader implications in oncology. https://doi.org/10.3390/ijms25052504

Causes of Low Milk Supply: The Roles of Estrogens, Progesterone, and Related External Factors,

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Advances in Nutrition 15, no. 1 (Jan 2024),

Low milk supply (LMS) poses a significant challenge to exclusive and continued breastfeeding, affecting similar to 10% to 15% of mothers. Milk production is intricately regulated by both endocrine and autocrine control mechanisms, with estrogens and progesterone playing pivotal roles in this process. In addition to endogenously produced hormones, external substances capable of interfering with normal hormonal actions, including phytoestrogens, mycoestrogens, synthetic estrogens, and hormonal contraceptives, can influence milk production. The effects of these extrinsic hormones on milk production may vary based on maternal body mass index. This comprehensive review examines the multifaceted causes of LMS, focusing on the involvement of estrogens, progesterone, and related external factors in milk production. Furthermore, it investigates the interplay between hormonal factors and obesity, aiming to elucidate the endocrine mechanisms underlying obesity-associated LMS. Insights from this review provide valuable perspectives for developing interventions to improve milk production and address the challenges associated with LMS. https://doi.org/10.1016/j.advnut.2023.10.002

Chemical contaminants in blood and their implications in chronic diseases,

ZHANG Y. Z., Y. R. GAO, Q. S. LIU, Q. F. ZHOU and G. B. JIANG,

Journal of Hazardous Materials 466 (Mar 2024),

Artificial chemical products are widely used and ubiquitous worldwide and pose a threat to the environment and human health. Accumulating epidemiological and toxicological evidence has elucidated the contributions of environmental chemical contaminants to the incidence and development of chronic diseases that have a negative impact on quality of life or may be life - threatening. However, the pathways of exposure to these chemicals and their involvements in chronic diseases remain unclear. We comprehensively reviewed the research progress on the exposure risks of humans to environmental contaminants, their body burden as indicated by blood monitoring, and the correlation of blood chemical contaminants with chronic diseases. After entering the human body through various routes of exposure, environmental contaminants are transported to target organs through blood circulation. The application of the modern analytical techniques based on human plasma or serum specimens is promising for determining the body burden of environmental contaminants, including legacy persistent organic pollutants, emerging pollutants, and inorganic elements. Furthermore, their body burden, as indicated by blood monitoring correlates with the incidence and development of metabolic syndromes, cancers, chronic nervous system diseases, cardiovascular diseases, and reproductive disorders. On this basis, we highlight the urgent need for further research on environmental pollution causing health problems in humans. https://doi.org/10.1016/j.jhazmat.2024.133511

Chemical mixture that targets the epidermal growth factor pathway impairs human trophoblast cell functions,

WAYE A. A., E. TICIANI and A. VEIGA-LOPEZ,

Toxicology and Applied Pharmacology 483 (Feb 2024),

Pregnant women are exposed to complex chemical mixtures, many of which reach the placenta. Some of these chemicals interfere with epidermal growth factor receptor (EGFR) activation, a receptor tyrosine kinase that modulates several placenta cell functions. We hypothesized that a mixture of chemicals (Chem-Mix) known to reduce EGFR activation (polychlorinated biphenyl (PCB)-126, PCB-153, atrazine, trans-nonachlor, niclosamide, and bisphenol S) would interfere with EGFR-mediated trophoblast cell functions. To test this, we determined the chemicals' EGFR binding ability, EGFR and downstream effectors activation, and trophoblast functions (proliferation, invasion, and endovascular differentiation) known to be regulated by EGFR in extravillous trophoblasts (EVTs). The Chem-Mix competed with EGF for EGFR binding, however only PCB-153, niclosamide, trans-non- achlor, and BPS competed for binding as single chemicals. The effects of the Chem-Mix on EGFR phosphorylation were tested by exposing the placental EVT cell line, HTR-8/SVneo to control (0.1% DMSO), Chem-Mix (1, 10, or 100 ng/ml), EGF (30 ng/ml), or Chem-Mix + EGF. The Chem-Mix - but not the individual chemicals - reduced EGF-mediated EGFR phosphorylation in a dose dependent manner, while no effect was observed in its downstream effectors (AKT and STAT3). None of the individual chemicals affected EVT cell invasion, but the ChemMix reduced EVT cell invasion independent of EGF. In support of previous studies that have explored chemicals targeting a specific pathway (estrogen/androgen receptor), current findings indicate that exposure to a chemical mixture that targets the EGFR pathway can result in a greater impact compared to individual chemicals in the context of placental cell functions. https://doi.org/10.1016/j.taap.2024.116804

Complex roles for sulfation in the toxicities of polychlorinated biphenyls,

DUFFEL M. W. and H. J. LEHMLER,

Critical Reviews in Toxicology 54, no. 2 (Feb 2024): 92-122,

Polychlorinated biphenyls (PCBs) are persistent organic toxicants derived from legacy pollution sources and their formation as inadvertent byproducts of some current manufacturing processes. Metabolism of PCBs is often a critical component in their toxicity, and relevant metabolic pathways usually include their initial oxidation to form hydroxylated polychlorinated biphenyls (OH-PCBs). Subsequent sulfation of OH-PCBs was originally thought to be primarily a means of detoxication; however, there is strong evidence that it may also contribute to toxicities associated with PCBs and OH-PCBs. These contributions include either the direct interaction of PCB sulfates with receptors or their serving as a localized precursor for OH-PCBs. The formation of PCB sulfates is catalyzed by cytosolic sulfotransferases, and, when transported into the serum, these metabolites may be retained, taken up by other tissues, and subjected to hydrolysis catalyzed by intracellular sulfatase(s) to regenerate OH-PCBs. Dynamic cycling between PCB sulfates and OH-PCBs may lead to further metabolic activation of the resulting OH-PCBs. Ultimate toxic endpoints of such processes may include endocrine disruption, neurotoxicities, and many others that are associated with exposures to PCBs and OH-PCBs. This review highlights the current understanding of the complex roles that PCB sulfates can have in the toxicities of PCBs and OH-PCBs and research on the varied mechanisms that control these roles. https://doi.org/10.1080/10408444.2024.2311270

Differential Disruption of Glucose and Lipid Metabolism Induced by Phthalates in Human Hepatocytes and White Adipocytes,

TIAN Y. R., M. XU, H. L. SHANG, L. J. YOU, J. YANG, X. D. JIA, H. YANG, Y. N. WU, X. F. YANG and Y. WAN,

Toxics 12, no. 3 (Mar 2024),

Phthalic acid esters (PAEs), commonly used as plasticizers, are pervasive in the environment, leading to widespread human exposure. The association between phthalate exposure and metabolic disorders has been increasingly recognized, yet the precise biological mechanisms are not well-defined. In this study, we explored the effects of monoethylhexyl phthalate (MEHP) and monocyclohexyl phthalate (MCHP) on glucose and lipid metabolism in human hepatocytes and adipocytes. In hepatocytes, MEHP and MCHP were observed to enhance lipid uptake and accumulation in a dose-responsive manner, along with upregulating genes involved in lipid biosynthesis. Transcriptomic analysis indicated a broader impact of MEHP on hepatic gene expression relative to MCHP, but MCHP particularly promoted the expression of the gluconeogenesis key enzymes G6PC and FBP1. In adipocytes, MEHP and MCHP both increased lipid droplet formation, mimicking the effects of the Peroxisome proliferator-activated receptor gamma (PPAR gamma) agonist rosiglitazone (Rosi). Transcriptomic analysis revealed that MEHP predominantly altered fatty acid metabolism pathways in mature adipocytes (MA), whereas MCHP exhibited less impact. Metabolic perturbations from MEHP and MCHP demonstrate shared activation of the PPARs pathway in hepatocytes and adipocytes, but the cell-type discrepancy might be attributed to the differential expression of PPAR gamma. Our results indicate that MEHP and MCHP disrupt glucose and lipid homeostasis in human liver and adipose through mechanisms that involve the PPAR and adenosine monophosphate-activated protein kinase (AMPK) signaling pathways, highlighting the nuanced cellular responses to these environmental contaminants. https://doi.org/10.3390/toxics12030214

Effects and mechanisms of bisphenols exposure on neurodegenerative diseases risk: A systemic review,

XU Y. Q., J. NIE, C. H. LU, C. HU, Y. L. CHEN, Y. MA, Y. R. HUANG and L. P. LU,

Science of the Total Environment 919 (Apr 2024),

Environmental bisphenols (BPs) pose a global threat to human health because of their extensive use as additives in plastic products. BP residues are increasing in various environmental media (i.e., water, soil, and indoor dust) and biological and human samples (i.e., serum and brain). Both epidemiological and animal studies have determined an association between exposure to BPs and an increased risk of neurodegenerative diseases (e.g., Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis), including cognitive abnormalities and behavioral disturbances. Hence, understanding the biological responses to different BPs is essential for prevention, and treatment. This study provides an overview of the underlying pathogenic molecular mechanisms as a valuable basis for understanding neurodegenerative disease responses to BPs, including accumulation of misfolded proteins, reduction of tyrosine hydroxylase and dopamine, abnormal hormone signaling, neuronal death, oxidative stress, calcium homeostasis, and inflammation. These findings provide new insights into the neurotoxic potential of BPs and ultimately contribute to a comprehensive health risk evaluation. https://doi.org/10.1016/j.scitotenv.2024.170670

Endocrine disrupting potential of total and bioaccessible extracts of dust from seven different types of indoor environment,

PINTO-VIDAL F. A., J. NOVÁK, S. R. JILKOVÁ, T. RUSINA, B. VRANA, L. MELYMUK and K. HILSCHEROVÁ,

Journal of Hazardous Materials 469 (May 2024),

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

Filling the Blank Space: Branched 4-Nonylphenol Isomers Are Responsible for Robust Constitutive Androstane Receptor (CAR) Activation by Nonylphenol,

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Environmental Science & Technology 58, no. 16 (Apr 2024): 6913-6923,

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

Glyphosate: Hepatotoxicity, Nephrotoxicity, Hemotoxicity, Carcinogenicity, and Clinical Cases of Endocrine, Reproductive, Cardiovascular, and Pulmonary System Intoxication,

MAZURYK J., K. KLEPACKA, W. KUTNER and P. S. SHARMA,

Acs Pharmacology & Translational Science (2024 Apr 2024),

Glyphosate (GLP) is an active agent of GLP-based herbicides (GBHs), i.e., broad-spectrum and postemergent weedkillers, commercialized by Monsanto as, e.g., Roundup and RangerPro formulants. The GBH crop spraying, dedicated to genetically engineered GLP-resistant crops, has revolutionized modern agriculture by increasing the production yield. However, abusively administered GBHs' ingredients, e.g., GLP, polyoxyethyleneamine, and heavy metals, have polluted environmental and industrial areas far beyond farmlands, causing global contamination and life-threatening risk, which has led to the recent local bans of GBH use. Moreover, preclinical and clinical reports have demonstrated harmful impacts of GLP and other GBH ingredients on the gut microbiome, gastrointestinal tract, liver, kidney, and endocrine, as well as reproductive, and cardiopulmonary systems, whereas carcinogenicity of these herbicides remains controversial. Occupational exposure to GBH dysregulates the hypothalamic-pituitary-adrenal axis, responsible for steroidogenesis and endocrinal secretion, thus affecting hormonal homeostasis, functions of reproductive organs, and fertility. On the other hand, acute intoxication with GBH, characterized by dehydration, oliguria, paralytic ileus, as well as hypovolemic and cardiogenic shock, pulmonary edema, hyperkalemia, and metabolic acidosis, may occur fatally. As no antidote has been developed for GBH poisoning so far, the detoxification is mainly symptomatic and supportive and requires intensive care based on gastric lavage, extracorporeal blood filtering, and intravenous lipid emulsion infusion. The current review comprehensively discusses the molecular and physiological basics of the GLP- and/or GBH-induced diseases of the endocrine and reproductive systems, and cardiopulmonary-, nephro-, and hepatotoxicities, presented in recent preclinical studies and case reports on the accidental or intentional ingestions with the most popular GBHs. Finally, they briefly describe modern and future healthcare methods and tools for GLP detection, determination, and detoxification. Future electronically powered, decision-making, and user-friendly devices targeting major GLP/GBH's modes of actions, i.e., dysbiosis and the inhibition of AChE, shall enable self-handled or point-of-care professional-assisted evaluation of the harm followed with rapid capturing GBH xenobiotics in the body and precise determining the GBH pathology-associated biomarkers levels. https://doi.org/10.1021/acsptsci.4c00046

The Hidden Threat: Endocrine Disruptors and Their Impact on Insulin Resistance,

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Cureus Journal of Medical Science 15, no. 10 (Oct 2023),

The association between Insulin resistance, a global health issue, and endocrine disruptors (EDCs), chemicals interfering with the endocrine system, has sparked concern in the scientific community. This article provides a comprehensive review of the existing literature regarding the intricate relationship between EDCs and insulin resistance. Phthalates, commonly found in consumer products, are well established EDCs with documented effects on insulin-signaling pathways and metabolic processes. Epidemiological studies have connected phthalate exposure to an increased risk of type 2 diabetes mellitus (T2DM). Perfluoroalkyl substances (PFAS), persistent synthetic compounds, have shown inconsistent associations with T2DM in epidemiological research.

However, studies suggest that PFAS may influence insulin resistance and overall metabolic health, with varying effects depending on specific PFAS molecules and study populations. Bisphenol A (BPA), found in plastics and resins, has emerged as a concern for glucose regulation and insulin resistance. Research has linked BPA exposure to T2DM, altered insulin release, obesity, and changes in the mass and function of insulin-secreting beta-cells. Triclosan, an antibacterial agent in personal care products, exhibits gender-specific associations with T2DM risk. It may impact gut microbiota, thyroid hormones, obesity, and inflammation, raising concerns about its effects on metabolic health. Furthermore, environmental EDCs like polycyclic aromatic hydrocarbons, pesticides, and heavy metals have demonstrated associations with T2DM, insulin resistance, hypertension, and obesity. Occupational exposure to specific pesticides and heavy metals has been linked to metabolic abnormalities. https://doi.org/10.7759/cureus.47282

The impact of endocrine-disrupting chemicals on stem cells: Mechanisms and implications for human health,

MUÑOZ J. P.,

Journal of Environmental Sciences 147 (Jan 2025): 294-309,

Endocrine-disrupting chemicals (EDCs) are compounds, either natural or man-made, that interfere with the normal functioning of the endocrine system. There is increasing evidence that exposure to EDCs can have profound adverse effects on reproduction, metabolic disorders, neurological alterations, and increased risk of hormone-dependent cancer. Stem cells (SCs) are integral to these pathological processes, and it is therefore crucial to understand how EDCs may influence SC functionality. This review examines the literature on different types of EDCs and their effects on various types of SCs, including embryonic, adult, and cancer SCs. Possible molecular mechanisms through which EDCs may influence the phenotype of SCs are also evaluated. Finally, the possible implications of these effects on human health are discussed. The available literature demonstrates that EDCs can influence the biology of SCs in a variety of ways, including by altering hormonal pathways, DNA damage, epigenetic changes, reactive oxygen species production and alterations in the gene expression pattems. These disruptions may lead to a variety of cell fates and diseases later in adulthood including increased risk of endocrine disorders, obesity, infertility, reproductive abnormalities, and cancer. Therefore, the review emphasizes the importance of raising broader awareness regarding the intricate impact of EDCs on human health. (c) 2024 The Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences. Published by Elsevier B.V. https://doi.org/10.1016/j.jes.2023.11.015

Impact of Exposure to a Mixture of Organophosphate Esters on Adrenal Cell Phenotype, Lipidome, and Function,

LI Z. X., B. F. HALES and B. ROBAIRE,

Endocrinology 165, no. 4 (Feb 2024),

Organophosphate esters (OPEs) are used primarily as flame retardants and plasticizers. Previously, we reported that adrenal cells are important targets of individual OPEs. However, real-life exposures are to complex mixtures of these chemicals. To address this, we exposed H295R human adrenal cells to varying dilutions (1/1000K to 1/3K) of a Canadian household dust-based OPE mixture for 48 hours and evaluated effects on phenotypic, lipidomic, and functional parameters. Using a high-content screening approach, we assessed phenotypic markers at mixture

concentrations at which there was greater than 70% cell survival; the most striking effect of the OPE mixture was a 2.5-fold increase in the total area of lipid droplets. We then determined the response of specific lipid species to OPE exposures with novel, nontargeted lipidomic analysis of isolated lipid droplets. These data revealed that house dust OPEs induced concentration-dependent alterations in the composition of lipid droplets, particularly affecting the triglyceride, diglyceride, phosphatidylcholine, and cholesterol ester subclasses. The steroid-producing function of adrenal cells in the presence or absence of a steroidogenic stimulus, forskolin, was determined. While the production of 17 beta-estradiol remained unaffected, a slight decrease in testosterone production was observed after stimulation. Conversely, a 2-fold increase in both basal and stimulated cortisol and aldosterone production was observed. Thus, exposure to a house dust-based mixture of OPEs exerts endocrine-disrupting effects on adrenal cells, highlighting the importance of assessing the effects of environmentally relevant mixtures. https://doi.org/10.1210/endocr/bqae024

Into the toxicity potential of an array of parabens by biomimetic liquid chromatography, cell viability assessments and in silico predictions,

NERI I., J. MACCALLUM, R. DI LORENZO, G. RUSSO, F. LYNEN and L. GRUMETTO,

Science of the Total Environment 917 (Mar 2024),

Five parabens (PBs) i.e., Methylparaben (MP), Ethylparaben (EP), Isopropylparaben (iPrP), Isobutylparaben (iBuP), Benzylparaben (BzP), and their parent compound i.e., para-hydroxy Benzoic Acid (pHBA), were studied both in vitro and in silico. Specifically, we determined their retention on several both protein- (Human Serum Albumin and alpha(1)-acidic glycoprotein) and (phospho) lipid-(immobilized artificial membrane (IAM)) based biomimetic stationary phases to evaluate their penetration potential through the biomembranes and their possible distribution in the body. The IAM phases were based either on phosphatidylcholine (PC) analogues i.e., PC.MG and PC.DD2 or on sphingomyelin (SPH). We also assessed their viability effect on breast cancer cells (MCF-7) via MTT assay subjecting the cells to five different PB concentrations i.e., 100 mu M, 10 mu M, 1 mu M, 0.1 mu M and 0.01 mu M. Finally, their pharmacokinetics and toxicity were assessed by the ADMET Predictor (TM) software. Isopropylparaben was found to be more active than 17 beta estradiol (E2) employed as positive control, on the screened cell line inducing cell proliferation up to 150 % more of untreated cells. Other analogues showed only a slight/moderate cell proliferation activity, with parabens having longer/branched side chain showing, on average, a higher proliferation rate. Significant linear direct relationships (for PC.DD2 $r(2) = 0.89$, $q(2) = 0.86$, for SPH $r(2) = 0.89$, $q(2) = 0.85$, for both P value < 0.05) were observed between the difference in proliferative effect between the readout and the control at 0.01 mu M concentration and the retention on the IAM phases measured at pH 5.0 for all compounds but pHBA, which is the only analyte of the dataset supporting a carboxylic acid moiety. IAM affinity data measured at pH 7.0 were found to be related to the effective human jejunal permeability as predicted by the software ADMET (R) Predictor, which is relevant when PBs are added to pharmaceutical and food commodities. https://doi.org/10.1016/j.scitotenv.2024.170461

Mechanism and impact of heavy metal-aluminum (Al) toxicity on male reproduction: Therapeutic approaches with some phytochemicals,

ALI F. E. M., K. S. A. BADRAN, M. A. BARAKA, H. S. ALTHAGAFY and E. H. M. HASSANEIN,

Life Sciences 340 (Mar 2024),

Heavy metals are ubiquitous environmental toxicants that have been known to have a serious effect on human and animal health. Aluminum (Al) is a widely distributed metal in nature. Al exposure has a detrimental impact on human fertility. This review focused on Al-induced male reproductive toxicity and the potential therapeutic approaches with some phytochemicals. Data from the literature showed that Al exposure is accompanied by a drastic decline in blood levels of FSH, LH, and testosterone, reduced sperm count, and affected sperm quality. Al exposure at high levels can cause oxidative stress by increasing ROS and RNS production, mediated mainly by downregulating Nrf2 signaling. Moreover, several investigations demonstrated that Al exposure evoked inflammation, evidenced by increased TNF-alpha and IL-6 levels. Additionally, substantial evidence concluded the key role of apoptosis in Al-induced testicular toxicity mediated by upregulating caspase-3 and downregulating Bcl2 protein. The damaging effects of Al on mitochondrial bioenergetics are thought to be due to the excessive generation of free radicals. This review helps to clarify the main mechanism involved in Al-associated testicular intoxication and the treatment strategy to attenuate the notable harmful effects on the male reproductive system. It will encourage clinical efforts to target the pathway involved in Al-associated testicular intoxication. https://doi.org/10.1016/j.lfs.2024.122461

Multiphase Ozonolysis of Bisphenol A: Chemical Transformations on Surfaces in the Environment,

YU J., Y. F. GONG, P. NAIR, J. LIGGIO, H. PENG and J. P. D. ABBATT,

Environmental Science & Technology 58, no. 8 (Feb 2024): 3931-3941,

High global plastic production volumes have led to the widespread presence of bisphenol compounds in human living and working environments. The most common bisphenol, bisphenol A (BPA), despite being endocrine disruptive and estrogenic, is still not fully banned worldwide, leading to continued human exposure via particles in air, dust, and surfaces in both outdoor and indoor environments. While its abundance is well documented, few studies have addressed the chemical transformations of BPA, the properties of its reactive products, and their toxicity. Here, the first gas-surface multiphase ozonolysis experiment of BPA thin films, at a constant ozone mixing ratio of 100 ppb, was performed in a flow tube for periods up to 24 h. Three transformation products involving the addition of 1, 2, and 3 oxygen atoms to the molecule were identified by LC-ESI-HRMS analyses. Exposure of indoor air to thin BPA surface films and BPA-containing thermal paper over periods of days validated the flow tube experiments, demonstrating the rapid nature of this multiphase ozonolysis reaction at atmospherically relevant ozone levels. Multiple transformation pathways are proposed that are likely applicable to not only BPA but also emerging commercial bisphenol products. https://doi.org/10.1021/acs.est.3c08932

Oestrogens, adipose tissues and environmental exposures influence obesity and diabetes across the lifecycle,

BARDHI O., P. DUBEY, B. F. PALMER and D. J. CLEGG,

Proceedings of the Nutrition Society (2024 Feb 2024),

Endogenous oestrogens regulate essential functions to include menstrual cycles, energy balance, adipose tissue distribution, pancreatic beta-cell function, insulin sensitivity and lipid homeostasis. Oestrogens are a family of hormones which include oestradiol (E2), oestrone (E1) and oestriol (E3). Oestrogens function by binding and activating oestrogen receptors (ERs). Phytoestrogens are plant-derived compounds which exhibit oestrogenic-like activity and can bind to ERs. Phytoestrogens

exert potential oestrogenic-like benefits; however, their effects are context-dependent and require cautious consideration regarding generalised health benefits. Xenoestrogens are synthetic compounds which have been determined to disrupt endocrine function through binding to ERs. Xenoestrogens enter the body through various routes and given their chemical structure they can accumulate, posing long-term health risks. Xenoestrogens interfere with endogenous oestrogens and their functions contributing to conditions like cancer, infertility, and metabolic disorders. Understanding the interplay between endogenous and exogenous oestrogens is critical in order to determine their potential health consequences and requires further investigation. This manuscript provides a summary of the role endogenous oestrogens have in regulating metabolic functions. Additionally, we discuss the impact phytoestrogens and synthetic xenoestrogens have on biological systems across various life stages. We highlight their mechanisms of action, potential benefits, risks and discuss the need for further research to bridge gaps in understanding and mitigate exposure-related health risks. https://doi.org/10.1017/s0029665124000119

An Overview of the Mechanisms of Cadmium-Induced Toxicity in the Male Reproductive System,

ANTAR S. A., A. HALOUANI, C. GAD and A. A. AL-KARMALAWY,

Pharmaceutical Sciences 30, no. 1 (Jan 2024): 36-53,

Cadmium (Cd) is a toxic heavy metal that is known to accumulate in various organs and tissues in the body, including the testes. Exposure to Cd has been shown to cause significant testicular damage, including impaired spermatogenesis and decreased fertility in both humans and animals. This damage is thought to be due to Cd-induced oxidative stress and inflammation, which can lead to cellular damage and apoptosis. Cd has also been shown to disrupt the bloodtestis barrier, leading to increased permeability and an altered testicular microenvironment. In addition, Cd exposure has been linked to changes in hormone levels, including decreased testosterone production and altered gonadotropin secretion. Reactive oxygen species (ROS) and an imbalance in the activity of antioxidant enzymes cause oxidative stress. The nuclear factor kappa-B (NF-kappa B) signaling system, which controls multiple genes involved in inflammatory responses including tumor necrosis factor (TNF-alpha), is activated by oxidative stress. These effects can contribute to decreased sperm count, motility, and viability. Efforts to reduce exposure to Cd may help to prevent or mitigate the harmful effects on testicular function. This can be achieved through occupational and environmental regulations, as well as public education and awareness programs. In this review, we highlight many of the principal mechanisms included in testicular damage. These pathways could be considered promising targets for the development of potential therapies for a variety of important human diseases. https://doi.org/10.34172/ps.2023.10

Plastic compounds and liver diseases: Whether bisphenol A is the only culprit,

SANGWAN S., R. BHATTACHARYYA and D. BANERJEE,

Liver International (2024 Feb 2024),

Plastics, while providing modern conveniences, have become an inescapable source of global concern due to their role in environmental pollution. Particularly, the focus on bisphenol A (BPA) reveals its biohazardous nature and association with liver issues, specifically steatosis. However, research indicates that BPA is just one facet of the problem, as other bisphenol analogues, microplastics, nanoplastics and additional plastic derivatives also pose potential risks. Notably, BPA is implicated in every stage of non-alcoholic fatty liver disease (NAFLD) onset and progression,

surpassing hepatitis B virus as a primary cause of chronic liver disease worldwide. As plastic contamination tops the environmental contaminants list, urgent action is needed to assess causative factors and mitigate their impact. This review delves into the molecular disruptions linking plastic pollutant exposure to liver diseases, emphasizing the broader connection between plastics and the rising prevalence of NAFLD. https://doi.org/10.1111/liv.15879

Recent advances of mass spectrometry-based analytical methods for endocrine disrupting chemicals in human matrices,

YUE M. J., X. L. ZHOU, J. T. FAN, S. GAO, X. E. ZHAO, S. Y. ZHU, Q. LIU and G. B. JIANG,

Trac-Trends in Analytical Chemistry 171 (Feb 2024),

Endocrine disrupting chemicals (EDCs), belonging to the category of emerging contaminants, are a class of highly heterogeneous persistent pollutants that can seriously interfere with the function of human endocrine system. Human matrices are extremely complex, and EDCs are usually present in trace concentrations and are often accompanied with analysis challenge due to their physical and chemical structure and properties. Therefore, sample preparation and analytical techniques are the key steps in the identification and quantitation of EDCs in human matrices. Mass spectrometry (MS) technique has powerful analytical performance, and is one of the preferred choices for EDCs. This review focused on 11 types of EDCs, including bisphenols, alkylphenols, phthalates, parabens, perfluorinated compounds, flame retardants, organic UV -filters, polycyclic aromatic hydrocarbons, pesticides, heavy metals, and some other concerned endocrine disruptors. The research progresses, advantages, disadvantages, and trends of sample preparation techniques and MS -based analytical methods for EDCs in human matrices were reviewed.
https://doi.org/10.1016/j.trac.2024.117523

Redox mechanisms of environmental toxicants on male reproductive function,

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Frontiers in Cell and Developmental Biology 12 (Feb 2024),

Humans and wildlife, including domesticated animals, are exposed to a myriad of environmental contaminants that are derived from various human activities, including agricultural, household, cosmetic, pharmaceutical, and industrial products. Excessive exposure to pesticides, heavy metals, and phthalates consequently causes the overproduction of reactive oxygen species. The equilibrium between reactive oxygen species and the antioxidant system is preserved to maintain cellular redox homeostasis. Mitochondria play a key role in cellular function and cell survival. Mitochondria are vulnerable to damage that can be provoked by environmental exposures. Once the mitochondrial metabolism is damaged, it interferes with energy metabolism and eventually causes the overproduction of free radicals. Furthermore, it also perceives inflammation signals to generate an inflammatory response, which is involved in pathophysiological mechanisms. A depleted antioxidant system provokes oxidative stress that triggers inflammation and regulates epigenetic function and apoptotic events. Apart from that, these chemicals influence steroidogenesis, deteriorate sperm quality, and damage male reproductive organs. It is strongly believed that redox signaling molecules are the key regulators that mediate reproductive toxicity. This review article aims to spotlight the redox toxicology of environmental chemicals on male reproduction function and its fertility prognosis. Furthermore, we shed light on the influence of redox signaling and

metabolism in modulating the response of environmental toxins to reproductive function. Additionally, we emphasize the supporting evidence from diverse cellular and animal studies. https://doi.org/10.3389/fcell.2024.1333845

The Role of Endocrine Disruption Chemical-Regulated Aryl Hydrocarbon Receptor Activity in the Pathogenesis of Pancreatic Diseases and Cancer,

KIM K.,

International Journal of Molecular Sciences 25, no. 7 (Apr 2024),

The aryl hydrocarbon receptor (AHR) serves as a ligand-activated transcription factor crucial for regulating fundamental cellular and molecular processes, such as xenobiotic metabolism, immune responses, and cancer development. Notably, a spectrum of endocrine-disrupting chemicals (EDCs) act as agonists or antagonists of AHR, leading to the dysregulation of pivotal cellular and molecular processes and endocrine system disruption. Accumulating evidence suggests a correlation between EDC exposure and the onset of diverse pancreatic diseases, including diabetes, pancreatitis, and pancreatic cancer. Despite this association, the mechanistic role of AHR as a linchpin molecule in EDC exposure-related pathogenesis of pancreatic diseases and cancer remains unexplored. This review comprehensively examines the involvement of AHR in EDC exposure-mediated regulation of pancreatic pathogenesis, emphasizing AHR as a potential therapeutic target for the pathogenesis of pancreatic diseases and cancer. https://doi.org/10.3390/ijms25073818

Screening for endocrine disrupting chemicals inhibiting monocarboxylate 8 (MCT8) transporter facilitated thyroid hormone transport using a modified nonradioactive assay,

WAGENAARS F., P. CENIJN, M. SCHOLZE, C. FRÄDRICH, K. RENKO, J. KÖHRLE and T. HAMERS,

Toxicology in Vitro 96 (Apr 2024),

Early neurodevelopmental processes are strictly dependent on spatial and temporally modulated of thyroid hormone (TH) availability and action. Thyroid hormone transmembrane transporters (THTMT) are critical for regulating the local concentrations of TH, namely thyroxine (T4) and 3,5,3 '-tri-iodothyronine (T3), in the brain. Monocarboxylate transporter 8 (MCT8) is one of the most prominent THTMT. Genetically induced deficiencies in expression, function or localization of MCT8 are associated with irreversible and severe neurodevelopmental adversities. Due to the importance of MCT8 in brain development, studies addressing chemical interferences of MCT8 facilitated T3 uptake are a crucial step to identify TH system disrupting chemicals with this specific mode of action. Recently a non-radioactive in vitro assay has been developed to rapidly screen for endocrine disrupting chemicals (EDCs) acting upon MCT8 mediated transport. This study explored the use of an UV -light digestion step as an alternative for the original ammonium persulfate (APS) digestion step. The non-radioactive TH uptake assay, with the incorporated UV -light digestion step of TH, was then used to screen a set of 31 reference chemicals and environmentally relevant substances to detect inhibition of MCT8-depending T3 uptake. This alternative assay identified three novel MCT8 inhibitors: methylmercury, bisphenol-AF and bisphenol-Z and confirmed previously known MCT8 inhibitors. https://doi.org/10.1016/j.tiv.2023.105770

Tetra methyl bisphenol F: another potential obesogen,

SINGH M., J. CROSTHWAIT, A. SORISKY and E. ATLAS,

International Journal of Obesity (2024 Feb 2024),

<bold>Background/objectives: </bold>Obesity and its associated metabolic diseases are increasing globally. Sedentary lifestyle, high caloric diet, and genetic predisposition are known to contribute to the onset of obesity. It is increasingly recognized that exposure to environmental chemicals such as Bisphenol A (BPA) may also play a significant role. BPA has been correlated with an array of adverse health effects, including obesity and metabolic disorders. Due to public concern, manufacturers are replacing BPA with structural analogues for which there is limited toxicological data. The objective of this study was to assess the effects of these BPA analogues on adipogenesis. <bold>Methods: </bold>The adipogenic effects of Tetra Methyl Bisphenol F (TMBPF), Bisphenol F (BPF), Bisphenol AP (BPAP), and fluorine-9-bisphenol (BHPF) were evaluated in murine 3T3-L1 cells. The cells were treated with BPA and its analogues at concentrations from 0.01 mu M to 20 mu M, throughout differentiation, in the absence of Dexamethasone (Dex). Lipid accumulation, mRNA and protein levels of adipogenic markers was assessed. <bold>Results: </bold>We found that TMBPF, BPF and BPA increased 3T3-L1 lipid accumulation and the expression levels of adipogenic markers lipoprotein lipase (Lpl), fatty acid binding protein 4 (Fabp4) and perilipin (Plin) (1-20 mu M; $p < 0.05$), whereas BHPF and BPAP had no effect in this model. Further, TMBPF induced adipogenesis to a greater extent than all the other chemicals including BPA (1-20 <mu>M; $p < 0.05$). The effect mediated by TMBPF on expression levels of Fabp4, but not Plin, is likely mediated via peroxisome proliferator-activated receptor (PPAR) gamma activation. <bold>Conclusions: </bold>Of the BPA analogues tested, BPF was most similar to BPA in its effects, while TMBPF was most adipogenic. In addition, TMBPF is likely a PPAR gamma agonist, it is likely an obesogenic chemical and may be a metabolic disruptor. https://doi.org/10.1038/s41366-024-01496-5

Triclosan and its alternatives, especially chlorhexidine, modulate macrophage immune response with distinct modes of action,

RAPS S., L. BAHR, I. KARKOSSA, M. ROSSOL, M. VON BERGEN and K. SCHUBERT,

Science of the Total Environment 914 (Mar 2024),

Since European regulators restricted the use of bacteriocidic triclosan (TCS), alternatives for TCS are emerging. Recently, TCS has been shown to reprogram immune metabolism, trigger the NLRP3 inflammasome, and subsequently the release of IL -18 in human macrophages, but data on substitutes is scarce. Hence, we aimed to examine the effects of TCS compared to its alternatives at the molecular level in human macrophages. LPS-stimulated THP-1 macrophages were exposed to TCS or its substitutes, including benzalkonium chloride, benzethonium chloride, chloroxylenol, chlorhexidine (CHX) and cetylpyridinium chloride, with the inhibitory concentration (IC10-value) of cell viability to decipher their mode of action. TCS induced the release of the proinflammatory cytokine TNF and high level of IL -18, suggesting the activation of the NLRP3-inflammasome, which was confirmed by non -apparent IL -18 under the NLRP3-inhibitor MCC950 treatment d. While IL -6 release was reduced in all treatments, the alternative CHX completely abolished the release of all investigated cytokines. To unravel the underlying molecular mechanisms, we used untargeted LC-MS/MS-based proteomics. TCS and CHX showed the strongest cellular response at the protein and signalling pathway level, whereby pathways related to metabolism, translation, cellular stress and migration were mainly affected but to different proposed modes of action. TCS inhibited mitochondrial electron transfer and affected phagocytosis. In contrast, in CHXtreated cells, the translation was arrested due to stress conditions, resulting in the formation of stress granules. Mitochondrial (e.g. ATP5F1D, ATP5PB, UQCRQ) and ribosomal (e.g. RPL10, RPL35, RPS23) proteins were revealed as putative key drivers. Furthermore, we have demonstrated the formation of podosomes by CHX, potentially involved in ECM degradation. Our results exhibit modulation of the

immune response in macrophages by TCS and its substitutes and illuminated underlying molecular effects. These results illustrate critical processes involved in the modulation of macrophages' immune response by TCS and its alternatives, providing information essential for hazard assessment. https://doi.org/10.1016/j.scitotenv.2023.169650

Méthodes

Deep eutectic solvents with solid supports used in microextraction processes applied for endocrine-disrupting chemicals,

GRAU J., A. CHABOWSKA, J. WERNER, A. ZGOLA-GRZESKOWIAK, M. FABJANOWICZ, N. JATKOWSKA, A. CHISVERT and J. PLOTKA-WASYLKA,

Talanta 268 (Feb 2024),

The determination of endocrine-disrupting chemicals (EDCs) has become one of the biggest challenges in Analytical Chemistry. Due to the low concentration of these compounds in different kinds of samples, it becomes necessary to employ efficient sample preparation methods and sensitive measurement techniques to achieve low limits of detection. This issue becomes even more struggling when the principles of the Green Analytical Chemistry are added to the equation, since finding an efficient sample preparation method with low damaging properties for health and environment may become laborious. Recently, deep eutectic solvents (DESs) have been proposed as the most promising green kind of solvents, but also with excellent analytical properties due to the possibility of custom preparation with different components to modify their polarity, viscosity or aromaticity among others. However, conventional extraction techniques using DESs as extraction solvents may not be enough to overcome challenges in analysing trace levels of EDCs. In this sense, combination of DESs with solid supports could be seen as a potential solution to this issue allowing, in different ways, to determine lower concentrations of EDCs. In that aim, the main purpose of this review is the study of the different strategies with solid supports used along with DESs to perform the determination of EDCs, comparing their advantages and drawbacks against conventional DES-based extraction methods. https://doi.org/10.1016/j.talanta.2023.125338

Determination of parabens in breast milk using stir bar sorptive extraction coupled with UHPLC-UV,

GE X., S. W. FENG, L. L. BIAN, M. J. WANG, K. F. LI and X. WANG,

Talanta 270 (Apr 2024),

We developed an analytical method based on ultra-high performance liquid chromatography with UV detection, using a stir bar coated with amino/hydroxyl bifunctional microporous organic network (B-MON), for the analysis of parabens in breast milk samples. B-MON demonstrated superior performance with maximal methylparaben adsorption of 112.15 mg/g. Kinetic fitting revealed that outer diffusion was the key limiting step, and the adsorption was chemisorption. The thermodynamic analysis demonstrated that increased methylparaben adsorption was found at higher temperatures in spontaneous processes. The developed approach showed excellent linearity (R2 >= 0.9964) and a low detection limit (0.01 mu g/L). Recoveries ranged from 85.8 to 105.5 % and the relative standard deviation was lower than 9.2 %. Based on the daily exposure assessment,

these pol-lutants do not pose unacceptable health hazards to babies. However, the high detection frequencies (41.9%-93.5 %) suggest that breast milk still should be monitored. https://doi.org/10.1016/j.talanta.2023.125609

Agenda

Rencontre scientifique. Perturbateurs endocriniens : les nouveaux défis de la recherche. 13 juin 2024. Maison de la RATP - 189 rue de Bercy - 75012 Paris
ANSES (2024),
L'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (Anses) et l'Agence nationale de la recherche (ANR) sont heureuses de vous inviter à leur deuxième rencontre scientifique consacrée aux perturbateurs endocriniens (PE). Programme : https://ptolemee.com/perturbateurs-endocriniens/programme.html https://ptolemee.com/perturbateurs-endocriniens/index.html

Ministère de transition écologique - Bilan de la seconde Stratégie nationale sur les perturbateurs endocriniens (SNPE 2)
12 juin 2024
Journée d'échange : stratégie nationale sur les perturbateurs endocriniens | Ministère de la Transition Écologique et de la Cohésion des Territoires https://www.ecologie.gouv.fr/journee-echange-strategie-nationale-perturbateurs-endocriniens

3ème congrès international PFAS "Gestion des risques environnementaux et sanitaires" - 4 au 6 juin 2024
Du 4 au 6 juin 2024, à Paris, cette 3ème édition du Congrès International sur les PFAS, sera une opportunité unique de rencontrer tous les acteurs concernés. https://www.webs-event.com/fr/event/PFAS/appelacom#aac

Congrès national de médecine et santé au travail 2024 (CNMST 24), symposium CARSAT/INRS sur les perturbateurs endocriniens 6 juin 2024
Le Congrès national de médecine et santé au travail qui se tient tous les deux ans, constitue l'occasion quasi unique de réunir en un seul lieu les acteurs des services de prévention et de santé au travail.https://www.medecine-sante-travail.com/

Webinar : Reducing PFAS in Products: Progress and Challenges . Pollution Prevention in Action: Webinar Series with EPA Office of Chemical Safety and Pollution Prevention,
US EPA O., *EPA* (8 mai 2024),
This May 8 webinar is sponsored by the U.S. Environmental Protection Agency (EPA). It will cover EPA's PFAS Strategic Roadmap and a new online tool for EPA's Recommendations of Specifications, Standards, and Ecolabels for Federal Purchasing that highlights how standards and ecolabels address PFAS. Speakers from EPA, EPA grantees, and Toxic-Free Future will discuss the progress they've made increasing the availability and use of products without PFAS, and the challenges that remain. https://www.epa.gov/p2/pollution-prevention-action-webinar-series-epa-office-chemical-safety-and-pollution-prevention

Endocrine disruptors and hormone levels during pregnancy. Webinar 7 may,
EHN (2024),

Can endocrine disrupting chemicals (EDCs) influence a mother's hormone levels during pregnancy? In this webinar, Brad Ryva and Dr. Diana Pacyga will discuss their recent study investigating this possibility in pregnant women enrolled in the Illinois Kids Development Study (I-KIDS). This is one of the first studies to investigate mixtures of EDCs and hormone levels during pregnancy. They studied known EDCs, including DEHP and bisphenol A (BPA), as well as chemicals used as replacements, such as DiNCH and bisphenol S (BPS). https://www.healthandenvironment.org/che-webinars/96754

Actualité, politique et évaluation de l'exposition

Le triphénylphosphate, un perturbateur endocrinien pour les espèces de l'environnement,

ANSES (10 avril 2024),

Le triphénylphosphate est une substance utilisée comme retardateur de flamme et/ou plastifiant dans de nombreux matériaux et équipements. Au vu de ses propriétés de perturbation endocrinienne pour des espèces de l'environnement, identifiées notamment sur les poissons, l'Agence propose d'identifier le triphénylphosphate comme substance extrêmement préoccupante, au sens du règlement européen REACH. Cela vise à mieux encadrer les utilisations de cette substance chimique sur le continent européen. Cette proposition de l'Anses est en consultation publique sur le site de l'ECHA, Agence européenne des produits chimiques, jusqu'au 15 avril afin de donner la possibilité aux parties prenantes de fournir des données complémentaires. https://www.anses.fr/fr/content/triphenylphosphate-pe-especes-environnement

Brain-harming chemicals seen in clearer light with fresh findings from the EURION Cluster - ERGO,

Ergo (29 fevrier 2024),

EU researchers have identified new ways that endocrine disrupting chemicals can interfere with people's hormone system and brain development. https://ergo-project.eu/brain-harming-chemicals-seen-in-clearer-light-with-fresh-findings-from-the-eurion-cluster/

Chemicals Used in Plastic Materials: An Estimate of the Attributable Disease Burden and Costs in the United States,

TRASANDE L., R. KRITHIVASAN, K. PARK, V. OBSEKOV and M. BELLIVEAU,

Journal of the Endocrine Society 8, no. 2 (Jan 2024),

Context Chemicals used in plastics have been described to contribute to disease and disability, but attributable fractions have not been quantified to assess specific contributions. Without this information, interventions proposed as part of the Global Plastics Treaty cannot be evaluated for potential benefits.Objective To accurately inform the tradeoffs involved in the ongoing reliance on plastic production as a source of economic productivity in the United States, we calculated the attributable disease burden and cost due to chemicals used in plastic materials in 2018.Methods We first analyzed the existing literature to identify plastic-related fractions (PRF) of disease and

disability for specific polybrominated diphenylethers (PBDE), phthalates, bisphenols, and polyfluoroalkyl substances and perfluoroalkyl substances (PFAS). We then updated previously published disease burden and cost estimates for these chemicals in the United States to 2018. By uniting these data, we computed estimates of attributable disease burden and costs due to plastics in the United States.Results We identified PRFs of 97.5% for bisphenol A (96.25-98.75% for sensitivity analysis), 98% (96%-99%) for di-2-ethylhexylphthalate, 100% (71%-100%) for butyl phthalates and benzyl phthalates, 98% (97%-99%) for PBDE-47, and 93% (16%-96%) for PFAS. In total, we estimate $249 billion (sensitivity analysis: $226 billion-$289 billion) in plastic-attributable disease burden in 2018. The majority of these costs arose as a result of PBDE exposure, though $66.7 billion ($64.7 billion-67.3 billion) was due to phthalate exposure and $22.4 billion was due to PFAS exposure (sensitivity analysis: $3.85-$60.1 billion).Conclusion Plastics contribute substantially to disease and associated social costs in the United States, accounting for 1.22% of the gross domestic product. The costs of plastic pollution will continue to accumulate as long as exposures continue at current levels. Actions through the Global Plastics Treaty and other policy initiatives will reduce these costs in proportion to the actual reductions in chemical exposures achieved. https://doi.org/10.1210/jendso/bvad163

Community Rolling Action Plan (CoRAP) update covering the years 2024, 2025 and 2026,

ECHA (19 mars 2024),

The Community rolling action plan (CoRAP) update for the years 2024-2026 lists 28 substances suspected of posing a risk to human health or the environment, for evaluation by 11 Member State Competent Authorities, under the substance evaluation process of the REACH Regulation (EC) No 1907/2006 (Articles 44 to 48). The plan contains 11 newly allocated substances and 17 substances already included in the previous CoRAP 2023-2025 update, published on 21 March 2023. Ten substances are planned to be evaluated in 2024, while 18 are listed for 2025 and 2026.

The initial ground for concern contains the notion of "potential endocrine disruptor" for 10 substances. https://echa.europa.eu/documents/10162/879660/corap_update_2024-2026_en.pdf/b0e44cd2-7abe-a148-97c6-a2042ded32bb#msdynttrid=pho-MXDshHJ17ih4v3tRuCdJ5diDw_tCs8yUBN5o7l4

European Medicines Agency Conflicts With the European Food Safety Authority (EFSA) on Bisphenol A Regulation,

ZOELLER R. T., L. S. BIRNBAUM, T. J. COLLINS, J. HEINDEL, P. A. HUNT, T. IGUCHI, A. KORTENKAMP, J. P. MYERS, F. S. VOM SAAL, C. SONNENSCHEIN and A. M. SOTO,

Journal of the Endocrine Society 7, no. 9 (Aug 2023),

The European Food Safety Authority (EFSA) has revised their estimate of the toxicity of bisphenol A (BPA) and, as a result, have recommended reducing the tolerable daily intake (TDI) by 20 000-fold. This would essentially ban the use of BPA in food packaging such as can liners, plastic food containers, and in consumer products. To come to this conclusion, EFSA used a systematic approach according to a pre-established protocol and included all guideline and nonguideline studies in their analysis. They found that Th-17 immune cells increased with very low exposure to

BPA and used this endpoint to revise the TDI to be human health protective. A number of regulatory agencies including the European Medicines Agency (EMA) have written formal disagreements with several elements of EFSA's proposal. The European Commission will now decide whether to accept EFSA's recommendation over the objections of EMA. If the Commission accepts EFSA's recommendation, it will be a landmark action using knowledge acquired through independent scientific studies focused on biomarkers of chronic disease to protect human health. The goal of this Perspective is to clearly articulate the monumental nature of this debate and decision and to explain what is at stake. Our perspective is that the weight of evidence clearly supports EFSA's proposal to reduce the TDI by 20 000-fold.
https://doi.org/10.1210/jendso/bvad107

Fatal feminisation: Problematising endocrine-disrupting chemicals in Denmark,

KROLOKKE C. H., A. N. BANG and K. HVIDTFELDT,

European Journal of Cultural Studies (2024 Feb 2024),

While an average everyday life in Denmark is vastly permeated with - and reliant upon - endocrine-disrupting chemicals; these invisible, yet active and mobile, compounds are often viewed as agents of disturbance causing harm in bodies and ecosystems as well as blurring boundaries upholding the two-sex system. In this article, we investigate how endocrine-disrupting chemicals came into existence as a problem for policy in Denmark. Drawing on a feminist cultural science studies framework and Carol Bacchi's 'What's the problem represented to be?' (WPR) analytical approach, we ask how endocrine-disrupting chemicals are problematised and what troubled figures emerge out of this problematisation for the Danish government and experts to address. Our analysis shows that endocrine-disrupting chemicals become embedded in a fear of feminisation that positions men, unborn children, and non-human (male) animals as potential victims of chemical exposure. Meanwhile, the female consumer and the woman/mother emerge as especially responsible for managing endocrine-disrupting chemicals. The article concludes that while feminisation is positioned as destabilising the social order, embodied by the nuclear family of fatally feminised figures, toxicity is constructed as transgressing interspecies, intergenerational and national borders.
https://doi.org/10.1177/13675494241229094

Les protections intimes sont-elles sans danger pour les femmes ?,

(2024-03-12 2024),

Ces dernières années, la question de la composition des protections intimes a suscité de nombreux débats publics en France. De plus en plus de femmes s'interrogent sur les risques liés à l'utilisation de ces articles d'hygiène féminine. Entre 2018 et 2020, l'Anses a réalisé une évaluation de la sécurité des protections intimes : les tampons, les serviettes hygiéniques, les protège-slips et les coupes menstruelles. Suite à cette évaluation et aux recommandations de l'Anses, les pouvoirs publics se sont saisis du sujet en 2022, et ont rédigé un décret sur l'étiquetage des protections féminines. https://www.anses.fr/fr/content/les-protections-intimes-sont-elles-sans-danger-pour-les-femmes

Next steps for PFAS restriction proposal,

ECHA (13 mars 2024),

The European Chemicals Agency (ECHA) outlines how its two scientific committees will progress in evaluating the proposal to restrict per- and polyfluoroalkyl substances (PFAS) in Europe. https://echa.europa.eu/fr/-/next-steps-for-pfas-restriction-proposal#msdynttrid=lwm8FNfF-3HcC-TPa0C4VKi_zX1w3au4978zpQxuI28

Nouveau plan PFAS : quelques avancées encore largement insuffisantes ! - Générations Futures,

(2024-04-11 2024),

Vendredi 5 avril, le gouvernement a publié un plan interministériel sur les PFAS. Générations Futures vous propose une analyse détaillée de ce nouveau plan interministériel qui présente, via plusieurs grands axes, les stratégies du gouvernement pour enfin gérer la problématique des polluants éternels. https://www.generations-futures.fr/actualites/nouveau-plan-pfas/

Perturbateurs endocriniens : la nécessité d'aller plus loin dans l'information des consommateurs - Générations Futures,

(2024-04-15 2024),

Les industriels sont désormais obligés de divulguer les informations sur la présence de perturbateurs endocriniens dans les produits de consommation https://www.generations-futures.fr/actualites/perturbateurs-endocriniens-affichage/

Perturbateurs endocriniens. Vers une meilleure prévention des expositions

BONVALLOT N. Rennes, Presses de l'EHESP.

Structuré en 19 fiches, ce guide propose des outils pratiques permettant de repérer ces substances chimiques, d'analyser les situations les plus à risque, et d'agir en matière de prévention pour réduire les expositions de la population.

Pfas ou polluants éternels et santé au travail : explications de l'INRS - Actualité - INRS,

Inrs (05 avril 2024),

Les Pfas sont des substances chimiques per- et polyfluoroalkylées. Dénommées « polluants éternels » du fait de leur persistance dans l'environnement, elles sont utilisées dans de nombreux secteurs d'activités en raison de leurs propriétés (antiadhésifs, ignifuges, antitaches, imperméabilisants, résistants aux fortes chaleurs…). Mais quels sont les risques encourus pour les travailleurs exposés ? Et quels sont les moyens de protection à mettre en œuvre ? Explications de Myriam Ricaud, experte d'assistance-conseil à l'INRS. https://www.inrs.fr/actualites/pfas-polluants-eternels-explications.html

The State of Research and Weight of Evidence on the Epigenetic Effects of Bisphenol A,

BESARATINIA A.,

International Journal of Molecular Sciences 24, no. 9 (Apr 2023),

Bisphenol A (BPA) is a high-production-volume chemical with numerous industrial and consumer applications. BPA is extensively used in the manufacture of polycarbonate plastics and epoxy resins. The widespread utilities of BPA include its use as internal coating for food and beverage cans, bottles, and food-packaging materials, and as a building block for countless goods of common use. BPA can be released into the environment and enter the human body at any stage during its production, or in the process of manufacture, use, or disposal of materials made from this chemical. While the general population is predominantly exposed to BPA through contaminated food and drinking water, non-dietary exposures through the respiratory system, integumentary system, and vertical transmission, as well as other routes of exposure, also exist. BPA is often classified as an endocrine-disrupting chemical as it can act as a xenoestrogen. Exposure to BPA has been associated with developmental, reproductive, cardiovascular, neurological, metabolic, or immune effects, as well as oncogenic effects. BPA can disrupt the synthesis or clearance of hormones by binding and interfering with biological receptors. BPA can also interact with key transcription factors to modulate regulation of gene expression. Over the past 17 years, an epigenetic mechanism of action for BPA has emerged. This article summarizes the current state of research on the epigenetic effects of BPA by analyzing the findings from various studies in model systems and human populations. It evaluates the weight of evidence on the ability of BPA to alter the epigenome, while also discussing the direction of future research.
https://doi.org/10.3390/ijms24097951

Thiaclopride : tout savoir sur ce pesticide dans le viseur du gouvernement français,

(2024),

Le Premier ministre, Gabriel Attal, veut empêcher l'importation en France de produits traités avec le thiaclopride. Utilisé pour certains fruits et légumes, ce pesticide est déjà interdit dans l'Union européenne. https://www.linfo.re/france/politique/thiaclopride-tout-savoir-sur-ce-pesticide-dans-le-viseur-du-gouvernement-francais

Towards a more effective REACH legislation in protecting human health,

GODDERIS L., E. DE RYCK, W. BAEYENS, L. GEERTS, G. JACOBS, P. MAESEN, B. MERTENS, G. SCHROYEN, F. VAN BELLEGHEM, J. VANOIRBEEK and N. VAN LAREBEKE,

Toxicological Sciences (2024 Feb 2024),

There is growing evidence indicating the substantial contribution of man-made products to an increase in the risk of diseases of civilization. In this article, the Belgian Scientific Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Committee gives a critical view on the working of REACH. The current regulatory framework needs to further evolve taking into account data generated using modern science and technology. There is a need for improved assessment process not only before but also after entering the market. Objectivity, transparency, and the follow-up after market access can be optimized. Additionally, no guidance documents exist for regulation of mixture effects. Further, the lengthiness before regulatory action is a big concern. Decision-making often takes several years leading to uncertainties for both producers and end users. A first proposed improvement is the implementation of independent toxicity testing, to assure objectivity, transparency, and check and improve compliance. A "no data, no market" principle could prevent access of hazardous chemicals to the market. Additionally, the introduction of novel testing could improve information on endpoints such as endocrine disrupting abilities, neurotoxicity, and immunotoxicity. An adapted regulatory framework that integrates data from

different sources and comparing the outputs with estimates of exposure is required. Fast toxicology battery testing and toxicokinetic testing could improve speed of decision-making. Hereby, several improvements have been proposed that could improve the current REACH legislation.
https://doi.org/10.1093/toxsci/kfae025

Toxicité sur les animaux

Dichloroacetic acid and trichloroacetic acid as disinfection by-products in drinking water are endocrine-disrupting chemicals,

CHEN W. N., X. Q. WANG, S. K. WAN, Y. YANG, Y. ZHANG, Z. Y. XU, J. S. ZHAO, C. Y. MI and H. D. ZHANG,

Journal of Hazardous Materials 466 (Mar 2024),

Dichloroacetic acid (DCAA) and trichloroacetic acid (TCAA) are two typical non-volatile disinfection by-products (DBPs) found in drinking water. Increasing evidence has demonstrated that they show reproductive toxicity. However, whether they might have endocrine disrupting properties remains largely unknown. To discover this, we treated male mice or pregnant mice with 0, 1-, 10(2)-, 10(3)-, 10(4)-, or 5 x 10(4)-fold maximal concentration level (MCL) of DCAA or TCAA in drinking water. In male mice, the levels of testosterone in serum and androgen receptor (AR) in testis were declined with >= 10(3)-fold MCL of DCAA (26.4 mg/kg/d) or TCAA (52.7 mg/kg/d). In pregnant mice, miscarriage rates were increased with >= 10(4)-fold MCL of DCAA (264 mg/kg/d) or >= 10(3)-fold MCL of TCAA. The levels of FSH in serum were increased and those of estradiol and progesterone were reduced with >= 10(3)-fold MCL of DCAA or TCAA. The protein levels of estrogen receptors (ER alpha and ER beta) in ovary were reduced with >= 10(2)-fold MCL of DCAA (2.64 mg/kg/d) or TCAA (5.27 mg/kg/d). Exposure to some certain fold MCL of DCAA or TCAA also altered the protein levels of ER alpha and ER beta in uterus and placenta. Exposure to 5 x 10(4)-fold MCL of both DCAA and TCAA showed the combined effects. Therefore, both DCAA and TCAA could be considered as novel reproductive endocrine disrupting chemicals, which might be helpful for further assessment of the toxicological effects of DCAA and TCAA and the awareness of reproductive endocrine disrupting properties caused by DCAA and TCAA in drinking water.
https://doi.org/10.1016/j.jhazmat.2023.133035

Early Developmental Exposure to Triclosan Impacts Fecal Microbial Populations, IgA and Functional Activities of the Rat Microbiome,

LAHIANI M., K. GOKULAN, V. SUTHERLAND, H. C. CUNNY, C. E. CERNIGLIA and S. KHARE,

Journal of Xenobiotics 14, no. 1 (Mar 2024): 193-213,

Triclosan (TCS), a broad-spectrum antibacterial chemical, is detected in human urine, breast milk, amniotic fluid, and feces; however, little is known about its impact on the intestinal microbiome and host mucosal immunity during pregnancy and early development. Pregnant female rats were orally gavaged with TCS from gestation day (GD) 6 to postpartum (PP) day 28. Offspring were administered TCS from postnatal day (PND) 12 to 28. Studies were conducted to assess changes in

the intestinal microbial population (16S-rRNA sequencing) and functional analysis of microbial genes in animals exposed to TCS during pregnancy (GD18), and at PP7, PP28 and PND28. Microbial abundance was compared with the amounts of TCS excreted in feces and IgA levels in feces. The results reveal that TCS decreases the abundance of Bacteroidetes and Firmicutes with a significant increase in Proteobacteria. At PND28, total Operational Taxonomic Units (OTUs) were higher in females and showed correlation with the levels of TCS and unbound IgA in feces. The significant increase in Proteobacteria in all TCS-treated rats along with the increased abundance in OTUs that belong to pathogenic bacterial communities could serve as a signature of TCS-induced dysbiosis. In conclusion, TCS can perturb the microbiome, the functional activities of the microbiome, and activate mucosal immunity during pregnancy and early development.
https://doi.org/10.3390/jox14010012

Effects of a TAML catalyst on mice exposed during pregnancy and lactation,

VANDENBERG L. N., J. P. MOGUS and G. K. SZABO,

Reproductive Toxicology 125 (Apr 2024),

Tetra-amido macrocyclic ligands (TAMLs) are catalysts designed to mimic endogenous peroxidases that can degrade pollutants. Before TAMLs gain widespread use, it is first important to determine if they have endocrine disrupting properties. In this study, we evaluated the effects of the iron TAML, NT7, on hormone-sensitive outcomes in mice exposed during pregnancy and lactation, and on their litters prior to weaning. We administered NT7 at one of three doses to mice via drinking water prior to and then throughout pregnancy and lactation. Two hormonally active pharmaceuticals, ethinyl estradiol (EE2) and flutamide (FLUT), a known estrogen receptor agonist and androgen receptor antagonist, respectively, were also included. In the females, we measured pre- and post-parturition weight, length of pregnancy, organ weights at necropsy, and morphology of the mammary gland at the end of the lactational period. We also quantified maternal behaviors at three stages of lactation. For the offspring, we measured litter size, litter weights, and the achievement of other developmental milestones. We observed only one statistically significant effect of NT7, a decrease in the percentage of pups with ear opening at postnatal day 5. This contrasts with the numerous effects of EE2 on both the mother and the litter, as well as several modest effects of FLUT. The approach taken in this study could provide guidance for future studies that aim to evaluate novel compounds for endocrine disrupting properties. https://doi.org/10.1016/j.reprotox.2024.108557

The Effects of Short- and Long-Term Ingestion of Plastic Toxin Bisphenol A on Gastrointestinal Transit Time in Rats,

DIXIT D., A. ROY, A. SHUKLA, P. SHARMA and M. MANDAL,

Cureus Journal of Medical Science 16, no. 2 (Feb 2024),

Introduction Exposure to bisphenol A (BPA), a toxic chemical released from plastic, affects various body functions, including reproduction, metabolism, and development. The most common route of exposure to BPA is oral, and the gastrointestinal (GI) tract is, therefore, the first body system to be exposed to BPA. BPA has been well -documented to impair gut contractility in rats, in vitro. It may therefore be hypothesized that BPA may adversely affect GI motility and hence slow down the movement of food, resulting in the increased transit of food bolus in the GI tract. There are no reports so far on the effects of BPA on GI transit time. Objectives The present study was undertaken to examine the impact of exposure to BPA by a single oral dose (termed as short-term

ingestion of BPA) and chronic (28 -day) oral dose (termed as long-term ingestion of BPA) on the transit time of food bolus in the gut of adult male albino rats. Methods and materials The study was conducted in the Department of Physiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India. In one set of experiments, each animal was fed a food pellet, once (short-term ingestion) containing BPA (2 mu g/kg and 50 mu g/kg in different groups), and in another set of experiments, each animal was fed a food pellet containing BPA (50 mu g/kg/day) for 28 consecutive days (longterm ingestion). Control rats in both sets were fed food pellets without BPA. Subsequently, the gastric transit index (GTI), ileocecal transit index (ICTI), and colonic transit time (CTT) were determined by the standard charcoal marker method. Results One-time ingestion of a food pellet containing BPA caused a significant ($p < 0.05$) drop in the GTI and ICTI and an increase in the CTT with both doses of BPA (2 and 50 mu g/kg). Similarly, after chronic (28 -day), oral BPA exposure, a significant decrease in the GTI and ICTT and an increase in CTT were observed. Conclusion Both short-term (one-time) and long-term (28 -day) oral exposure to BPA-containing food harmed GI transit. Slow GI transit may lead to metabolic disorders and GI motility disorders, such as constipation. https://doi.org/10.7759/cureus.53694

Environmental chemical TCPOBOP exposure alters milk liposomes and offspring growth trajectories in mice,

PAN S. J., W. YU, J. ZHANG, Y. GUO, X. X. QIAO, P. F. XU and Y. G. ZHAI,

Ecotoxicology and Environmental Safety 272 (Mar 2024),

Exposure to environmental endocrine disruptors (EEDs) has become a global health concern, and EEDs are known to be potent inducers of constitutive androstane receptor (CAR). 1,4-bis [2-(3,5-dichloropyridyloxy)] benzene (TCPOBOP, hereafter abbreviated as TC), a specific ligand for CAR, has been considered as a potential EED. Here, we analyzed the effect of TC exposure to female mice on the histological morphology of their alveoli in the basic unit of lactation. We quantified differences in the milk metabolome of the control and TC-exposed group while assessing the correlations between metabolites and neonatal growth. Mammary histological results showed that TC exposure inhibited alveolar development. Based on the milk metabolomic data, we identified a total of 1505 differential metabolites in both the positive and negative ion mode, which indicated that TC exposure affected milk composition. As expected, the differential metabolites were significantly enriched in the drug metabolism pathway. Further analyses revealed that differential metabolites were significantly enriched in multiple lipid metabolic pathways, such as fatty acid biosynthesis, suggesting that most differential metabolites were concentrated in lipids. Simultaneously, a quantitative analysis showed that TC exposure led to a decrease in the relative abundance of total milk lipids, affecting the proportion of some lipid subclasses. Notably, a portion of lipid metabolites were associated with neonatal growth. Taken together, these findings suggest that TC exposure may affect milk lipidomes, resulting in the inability of mothers to provide adequate nutrients, ultimately affecting the growth and health of their offspring.
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Maternal oral exposure to low-dose BPA accelerates the onset of puberty by promoting prepubertal Kiss1 expression in the AVPV nucleus of female offspring,

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Reproductive Toxicology 124 (Mar 2024),

As the incidence of precocious puberty has risen in recent years and the age at puberty onset is younger, children may be at increased risk for health consequences associated with the early onset of puberty. Bisphenol A (BPA) is recognized as an endocrine disruptor chemical that is reported to induce precocious puberty. The effect of BPA exposure modes, times, and doses (especially low dose) were controversial. In the present study, we evaluated the potential effects of maternal exposure to low-dose BPA on the hypothalamus, particularly on the arcuate (ARC) nucleus and anteroventral periventricular (AVPV) nucleus during peri-puberty in offspring of BPA-treated rats. Pregnant rats were exposed to corn oil vehicle, 0.05 mg center dot kg(-1)center dot day(-1) BPA, or 5 mg center dot kg(-1)center dot day(-1) from gestation day 1 (GD1) to postnatal day 21 (PND21) by daily gavage. Body weight (BW), vaginal opening (VO), ovarian follicular luteinization, and relevant hormone concentrations were measured; hypothalamic Kiss1 and GnRH1 levels by western immunoblot analysis were also assessed as indices of puberty onset. During or after exposure, low-dose BPA restricted BW after birth (at PND1 and PND5), and subsequently accelerated puberty onset by promoting the expression of prepubertal Kiss1 and GnRH1 in the AVPV nucleus on PND30, leading to advanced VO, an elevation in LH and FSH concentrations (on PND30). We also noted increased BW on PND30 and PND35. Maternal oral exposure to low-dose BPA altered the BW curve during the neonatal and peripubertal periods, and subsequently accelerated puberty onset by promoting prepubertal Kiss1 expression in the AVPV nucleus.
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Prenatal exposure to Di(2-ethylhexyl) phthalate and high-fat diet synergistically disrupts gonadal function in male mice,

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Biology of Reproduction (2024 Feb 2024),

Prenatal exposure to Di (2-ethylhexyl) phthalate (DEHP) impairs the reproductive system and causes fertility defects in male offspring. Additionally, high-fat (HF) diet is a risk factor for reproductive disorders in males. In this study, we tested the hypothesis that prenatal exposure to a physiologically relevant dose of DEHP in conjunction with HF diet synergistically impacts reproductive function and fertility in male offspring. Female mice were fed a control or HF diet 7 days prior to mating and until their litters were weaned on postnatal day 21. Pregnant dams were exposed to DEHP or vehicle from gestational day 10.5 until birth. The male offspring's gross phenotype, sperm quality, serum hormonal levels, testicular histopathology, and testicular gene expression pattern were analyzed. Male mice born to dams exposed to DEHP + HF had smaller testes, epididymides, and shorter anogenital distance compared with those exposed to HF or DEHP alone. DEHP + HF mice had lower sperm concentration and motility compared with DEHP mice. Moreover, DEHP + HF mice had more apoptotic germ cells, fewer Leydig cells, and lower serum testosterone levels than DEHP mice. Furthermore, testicular mRNA expression of Dnmt1 and Dnmt3a was two to eight-fold higher than in DEHP mice by qPCR, suggesting that maternal HF diet and prenatal DEHP exposure additively impact gonadal function by altering the degree of DNA methylation in the testis. These results suggest that the combined exposure to DEHP and high-fat synergistically impairs reproductive function in male offspring, greater than exposure to DEHP or HF diet alone. The combined exposure to DEHP and high-fat synergistically impairs reproductive function in maleoffspring, greater than exposure to DEHP or HF diet alone. [GRAPHICS] .
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Thiacloprid impairs reproductive functions of male Wistar rats,

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Naunyn-Schmiedebergs Archives of Pharmacology (2024 Mar 2024),

Global male infertility correlated to the rise of endocrine-disrupting chemicals, including insecticides, has grown into a pressing problem. Thiacloprid is one of the most commonly used neonicotinoids that accounts for more than 25% of the global pesticide industry. However, its impact on the reproductive system and male fertility has not been fully elucidated. The object of this study was to explore the adverse effects of thiacloprid on male Wistar rats' reproductive system. Thirty healthy male rats were separated into one of three groups: control group, and two groups that were orally administered with low (22.5 mg/kg) and high dose (62.1 mg/kg) of thiacloprid for 56 days. Thiacloprid significantly ($p<0.05$) reduced body weight and relative testicular weight, as well as sperm quality (count, motility, viability, and morphology), in a dose-dependent manner. THIA-treated groups revealed a large effect ($d > 0.8$) on semen quality with Cohen's d of (6.57, 8.82), (20.14, 23.54), and (2.81, 9.10) for count, motility, and viability respectively. Meanwhile, the serum testosterone level dropped while the levels of luteinizing and follicle-stimulating hormones increased. 17 beta-hydroxy steroid dehydrogenase and 3 beta-hydroxy steroid dehydrogenase levels were significantly decreased in a dose-dependent manner. The activity of the tested antioxidant enzymes catalase (CAT), glutathione reduced (GSH), and superoxide dismutase (SOD) exhibited a considerable decrease compared to the control group with a significant elevation in the lipid peroxidation activity as indicated by malondialdehyde (MDA) level. The testicular histology revealed degenerative changes in spermatogenic cells and interstitial tissue. Comet assay revealed DNA fragmentation in treated groups' testicular tissue. Thiacloprid exposure interferes with reproductive function and impairs male Wistar rat fertility. Such harmful consequences may also develop in humans frequently exposed to thiacloprid.
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