

# Bulletin Board

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## Technical

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## CHEMICAL EFFECTS

## Endocrine-Disrupting Chemicals: Introduction to the Theme

2021-04-13

Background: Endocrine-disrupting chemicals (EDCs) are natural or synthetic compounds deriving from different human activities and are widely spread into the environment, contributing to indoor and outdoor pollution. EDCs may be conveyed by food and water consumption and skin, airways, placental, and breastfeeding. Upon entering the circulation, they can interfere with endocrine system homeostasis by several mechanisms.

Aim: In this narrative review, the authors overviewed the leading mechanisms by which EDCs interact and disrupt the endocrine system, leading to possible human health concerns.

Results: The leading mechanisms of EDCs-related toxicity have been illustrated in in vitro studies and animal models and may be summarized as follows: receptor agonism and antagonism; modulation of hormone receptor expression; interference with signal transduction in hormone-responsive cells; epigenetic modifications in hormone-producing or hormone-responsive cells; interference with hormone synthesis; interference with hormone transport across cell membranes; interference with hormone metabolism or clearance; interference with the destiny of hormone-producing or hormone-responsive cells.

Discussion: Despite these well-defined mechanisms, some limitations do not allow for conclusive assumptions. Indeed, epidemiological and ecological studies are currently lacking and usually refer to a specific cluster of patients (occupational exposure). Methodological aspects could further complicate the issue since these studies could require a long time to provide useful information. The lack of a real unexposed group in environmental conditions, possible interference of EDCs mixture on biological results, and unpredictable dose-response curves for some EDCs should also be considered significant limitations.

Conclusion: Given these limitations, specific observational and long-term studies are needed to identify at-risk populations for adequate treatment of exposed patients and effective prevention plans against excessive exposure to EDCs.

Authors: Giuseppe Lisco, Vito Angelo Giagulli, Michele Iovino, Edoardo Guastamacchia, Giovanni De Pergola, Vincenzo Triggiani

Full Source: Endocrine, metabolic & immune disorders drug targets 2021 Apr 13. doi: 10.2174/1871530321666210413124425.

Background: Endocrine-disrupting chemicals (EDCs) are natural or synthetic compounds deriving from different human activities and are widely spread into the environment, contributing to indoor and outdoor pollution.

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## A preliminary study on the mechanism of the neurosteroid-mediated ionotropic receptor dysfunction in neurodevelopmental toxicity induced by decabromodiphenyl ether

2021-04-13

The mechanism of neurodevelopmental toxicity of decabromodiphenyl ether (BDE209) remains unclear. Recent evidence suggests that neurosteroids disorders play a vital role in BDE209 induced-neurodevelopmental toxicity. To explore the mechanism of it, pregnant ICR mice were orally gavaged with 0, 225, and 900 mg kg<sup>-1</sup> BDE209 for about 42 days. Spatial learning and memory abilities of offspring were tested on postnatal day (PND) 21. Offspring were euthanized at PND26, the neuronal structure, neurosteroids level, and related proteins including neurosteroids synthase, ionotropic receptors and cAMP-response element binding protein (CREB) pathway were evaluated, as well as Ca<sup>2+</sup> concentration and the mitochondrial membrane potential (Mmp). Our results showed that BDE209 impaired learning and memory abilities and disrupted neuronal structure. Meanwhile, BDE209 decreased the pregnenolone (PREG), dehydroepiandrosterone (DHEA), progesterone (PROG) and allopregnanolone (ALLO) levels in the serum and brain, as well as the mRNA and protein levels of cholesterol-side-chain cleavage enzyme (P450<sub>scc</sub>), steroid 17 $\alpha$ -hydroxylase (P450<sub>C17</sub>), 3 $\beta$ -hydroxysteroid dehydrogenase (3 $\beta$ -HSD) and steroid 5 $\alpha$ -reductase of type I (5 $\alpha$ -R) in the hippocampi. Also, BDE209 suppressed mRNA and protein levels of NR1, NR2A and NR2B subunits of the N-methyl-D-aspartic acid receptor (NMDAR) and  $\alpha$ 1 subunit of the Gamma-amino butyric acid A receptor (GABAAR), but increased the levels of  $\beta$ 2 and  $\gamma$ 2 subunits of the GABAAR in the hippocampi. Moreover, BDE209 increased the Ca<sup>2+</sup> concentration and phosphorylation extracellular regulated protein kinases (P-ERK) 1/2 level, but decreased the P-CREB and Mmp level in the hippocampi. These results indicate that BDE209 exposure during pregnancy and lactation is possible to affect learning and memory formation of offspring by the neurosteroid-mediated ionotropic receptors dysfunction.

Authors: Bo Qian, Zeng Zen, Zhaoxuan Zheng, Chengqiang Wang, Jiale Song

Full Source: Ecotoxicology and environmental safety 2021 Apr 13;217:112198. doi: 10.1016/j.ecoenv.2021.112198.

The mechanism of neurodevelopmental toxicity of decabromodiphenyl ether (BDE209) remains unclear.



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## ENVIRONMENTAL RESEARCH

## Environmental and Occupational Considerations of Anesthesia: A Narrative Review and Update

2021-04-15

With an estimated worldwide volume of 266 million surgeries in 2015, the call for general inhalation anesthesia is considerable. However, widely used volatile anesthetics such as N<sub>2</sub>O and the highly fluorinated gases sevoflurane, desflurane, and isoflurane are greenhouse gases, ozone-depleting agents, or both. Because these agents undergo minimal metabolism in the body during clinical use and are primarily ( $\geq 95\%$ ) eliminated unchanged via exhalation, waste anesthetic gases (WAGs) in operating rooms and postanesthesia care units can pose a challenge for overall elimination and occupational exposure. The chemical properties and global warming impacts of these gases vary, with atmospheric lifetimes of 1-5 years for sevoflurane, 3-6 years for isoflurane, 9-21 years for desflurane, and 114 years for N<sub>2</sub>O. Additionally, the use of N<sub>2</sub>O as a carrier gas for the inhalation anesthetics and as a supplement to intravenous (IV) anesthetics further contributes to these impacts. At the same time, unscavenged WAGs can result in chronic occupational exposure of health care workers to potential associated adverse health effects. Few adverse effects associated with WAGs have been documented, however, when workplace exposure limits are implemented. Specific measures that can help reduce occupational exposure and the environmental impact of inhaled anesthetics include efficient ventilation and scavenging systems, regular monitoring of airborne concentrations of waste gases to remain below recommended limits, ensuring that anesthesia equipment is well maintained, avoiding desflurane and N<sub>2</sub>O if possible, and minimizing fresh gas flow rates (eg, use of low-flow anesthesia). One alternative to volatile anesthetics may be total intravenous anesthesia (TIVA). While TIVA is not associated with the risks of occupational exposure or atmospheric pollution that are inherent to volatile anesthetic gases, clinical considerations should be weighed in the choice of agent. Appropriate procedures for the disposal of IV anesthetics must be followed to minimize any potential for negative environmental effects. Overall, although their contributions are relatively low compared with those of other human-produced substances, inhaled anesthetics are intrinsically potent greenhouse gases and pose a risk to operating-room personnel if not

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properly managed and scavenged. Factors to reduce waste and minimize the future impact of these substances should be considered.

Authors: Shane Varughese, Raza Ahmed

Full Source: Anesthesia and analgesia 2021 Apr 15. doi: 10.1213/ANE.0000000000005504.

## The Role of Behavioral Ecotoxicology in Environmental Protection

2021-04-14

For decades, we have known that chemicals affect human and wildlife behavior. Moreover, due to recent technological and computational advances, scientists are now increasingly aware that a wide variety of contaminants and other environmental stressors adversely affect organismal behavior and subsequent ecological outcomes in terrestrial and aquatic ecosystems. There is also a groundswell of concern that regulatory ecotoxicology does not adequately consider behavior, primarily due to a lack of standardized toxicity methods. This has, in turn, led to the exclusion of many behavioral ecotoxicology studies from chemical risk assessments. To improve understanding of the challenges and opportunities for behavioral ecotoxicology within regulatory toxicology/risk assessment, a unique workshop with international representatives from the fields of behavioral ecology, ecotoxicology, regulatory (eco)toxicology, neurotoxicology, test standardization, and risk assessment resulted in the formation of consensus perspectives and recommendations, which promise to serve as a roadmap to advance interfaces among the basic and translational sciences, and regulatory practices.

Authors: Alex T Ford, Marlene Ågerstrand, Bryan W Brooks, Joel Allen, Michael G Bertram, Tomas Brodin, ZhiChao Dang, Sabine Duquesne, René Sahm, Frauke Hoffmann, Henner Hollert, Stefanie Jacob, Nils Klüver, James M Lazorchak, Mariana Ledesma, Steven D Melvin, Silvia Mohr, Stephanie Padilla, Gregory G Pyle, Stefan Scholz, Minna Saaristo, Els Smit, Jeffery A Stevens, Sanne van den Berg, Werner Kloas, Bob B M Wong, Michael Ziegler, Gerd Maack

Full Source: Environmental science & technology 2021 Apr 14. doi: 10.1021/acs.est.0c06493.

For decades, we have known that chemicals affect human and wildlife behavior.



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**Associations between air pollution exposure and birth defects: a time series analysis**

2021-04-17

Air pollution is a serious environmental problem in China. Birth defects are particularly vulnerable to outdoor air pollution. Our study was to evaluate the association between short-term exposure to air pollutants and the risk of birth defects. Daily data including the air pollutants, meteorological characteristics, and birth records were obtained in Hefei, China, during January 2013 to December 2016. The findings showed that PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub> exposures were positively correlated with the risk of birth defects. Maternal exposure to PM<sub>2.5</sub> and SO<sub>2</sub> during the 4th to 13th gestational weeks was observed to have a significant association with the risk of birth defects, with the maximum effect in the 7th or 8th week for PM<sub>2.5</sub> and the maximum effect in the 7th week for SO<sub>2</sub>. The positively significant exposure windows were the 4th to 14th weeks for PM<sub>10</sub>, the 4th to 12th weeks for NO<sub>2</sub>, and the 26th to 35th weeks for O<sub>3</sub>, respectively. The strongest associations were observed in the 8th week for PM<sub>10</sub>, the 7th week for NO<sub>2</sub>, and in the 31st or 32nd week for O<sub>3</sub>. The findings of this study demonstrate that air pollutants increase the risk of birth defects among women during pregnancy in Hefei, China, which provide evidence for improving the health of pregnant women and neonates in developing countries, and uncovered potential opportunities to reduce or prevent birth defects by proactive measures during pregnancy.

Authors: Shu Sun, Qi Zhang, Xinmiao Sui, Liu Ding, Jie Liu, Mei Yang, Qihong Zhao, Chao Zhang, Jiahu Hao, Xiujun Zhang, Shilei Lin, Rui Ding, Jiyu Cao

Full Source: Environmental geochemistry and health 2021 Apr 17. doi: 10.1007/s10653-021-00886-2.

## OCCUPATIONAL

**The legacy of weapons grade plutonium production: Health status of Hanford complex workers who manage the waste**

2021-04-15

The extent and etiology of health effects in workers who maintain underground storage tanks at the Hanford Nuclear Reservation (Hanford) have been subjects of controversy and concern for several decades. Hanford is a decommissioned nuclear production complex managed by the US Department of Energy in southeast Washington State. This

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integration-of-evidence review evaluates the relationship between exposure to vapors from mixed chemical and radioactive waste stored in underground storage tanks at Hanford and worker health. Hanford workers' health information was gathered from technical reports, media reports, and published literature, including the systematic search of seven databases. This review describes the health status and health concerns of Hanford tank farm workers based on the integration of the available health effects data from disparate sources. In interviews with external groups, Hanford workers reported both irritant-type symptoms and diseases that they believe are attributable to tank farm vapors. However, the results of this integration-of-evidence review indicated that no pervasive pattern of occupational disease was identified that can be associated with exposure to tank farm vapors. Inhalation exposure to asbestos and beryllium is associated with lung disease from various types of nuclear industry work but not from work on tank farms. This review concluded that while irritant-type symptoms and isolated cases of occupational disease are plausible under certain conditions, the currently available data do not support a pervasive pattern of occupational disease associated with vapor exposure.

Authors: Debra Cherry, Elizabeth Friedman, Melissa Vincent, Andrew Maier  
Full Source: Toxicology and industrial health 2021 Apr 15;748233721996555. doi: 10.1177/0748233721996555.

**Risk assessment of workers' exposure to BTEX and hazardous area classification at gasoline stations**

2021-04-15

Vaporization of benzene, toluene, ethylbenzene, and xylene (BTEX) compounds pollutes the air and causes health hazards at gasoline stations. This study revealed the risk of BTEX exposure according to the hazardous area classification at gasoline stations. The risk assessment of gasoline workers from a representative group of 47 stations, which followed the United States Environmental Protection Agency-IRIS method of assessing BTEX exposure, was expressed as the hazard index (HI). A result of matrix multipliers of the hazardous exposure index and fire possibility from flammable gas classified hazardous area-I and area-II at the fuel dispensers. BTEX concentrations were actively sampled in ambient air and a flammable gas detector was used to measure the flammability level. Results showed that the BTEX concentrations from ambient air monitoring were in the range of 0.1-136.9, 8.1-406.0, 0.8-24.1 and 0.4-105.5 ppb for benzene, toluene, ethylbenzene, and xylene, respectively, which exceeded the NIOSH exposure limit of 100 ppb of benzene concentration. The risk assessment indicated that five stations reached an unacceptable risk

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of worker exposure to BTEX (HI>1), which correlated with the numbers of gasoline dispensers and daily gasoline sold. The risk matrix classified hazardous area-I at 4 meters and hazardous area-II at 4-8 meters in radius around the fuel dispensers. This study revealed the hazardous areas at gasoline stations and suggests that entrepreneurs must strictly control the safety operation practice of workers, install vapor recovery systems on dispenser nozzles to control BTEX vaporization and keep the hazardous areas clear of fire ignition sources within an eight-meter radius of the dispensers.

Authors: Sunisa Chaiklieng

Full Source: PloS one 2021 Apr 15;16(4):e0249913. doi: 10.1371/journal.pone.0249913.

### Biomonitoring of occupational exposure to bisphenol A, bisphenol S and bisphenol F: A systematic review

2021-04-05

Bisphenol A (BPA) and its substitutes bisphenol S (BPS) and bisphenol F (BPF) are endocrine disrupting chemicals widely used in the production of polycarbonate plastics, epoxy resins and thermal papers. The aim of the review was to identify occupational studies using human biomonitoring (HBM) as a tool for bisphenol exposure assessment and to characterize research gaps on the topic as part of the HBM4EU project. Hence, a systematic literature search using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology was conducted for articles published between 2000 and 27th March 2020 across three databases (PubMed, Scopus and Web of Science). Thirty studies on the occupational HBM of BPA met the inclusion criteria. Regarding BPS and BPF, only 4 and 2 publications were retrieved, respectively. Fifty-seven percent (57%) of the studies selected for BPA were conducted in Asia whereas half of BPS and BPF studies were undertaken in Europe. Studies on BPA in plastic and epoxy resin sectors were infrequent in Europe while Asian data showed higher exposure when the substance is employed as raw material. The main data on BPS were among cashiers while BPF data were available from incinerator workers. Several research gaps have been identified: (i) shortage of HBM studies on occupational exposure, especially to BPS and BPF; (ii) different methodological designs making suitable comparisons between studies difficult; and (iii) only few studies conducted on the industrial applications of bisphenols outside Asia. This review highlights the lack of recent occupational HBM studies on bisphenols and the need for a harmonized approach to acquire reliable data. Considering the increasing replacement of BPA by BPS and BPF, it is

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of relevance to evaluate the exposure to these substances and the impact of the available risk management measures on workers exposure and possible health risk.

Authors: Radia Bousoumah, Veruscka Leso, Ivo Iavicoli, Pasi Huuskonen, Susana Viegas, Simo P Porras, Tiina Santonen, Nadine Frery, Alain Robert, Sophie Ndaw

Full Source: The Science of the total environment 2021 Apr 5;783:146905. doi: 10.1016/j.scitotenv.2021.146905.

### The impact of chronic co-exposure to different heavy metals on small fibers of peripheral nerves. A study of metal industry workers

2021-04-15

Background: Chronic exposure to heavy metals affects various organs, among them the brain and peripheral nerves. Polyneuropathy is mainly length-dependent with predominantly sensory symptoms. There have been few studies on small fiber neuropathy due to heavy metal intoxication. Methods: We investigated 41 metal industry workers, mean age  $51.3 \pm 10.5$  years, with at least 5 years' professional exposure to heavy metals, and 36 age- and sex-matched healthy controls. We performed neurological examinations, and assessed blood levels of cadmium, lead, and zinc protoporphyrin, urine levels of arsenic, standard, sensory and motor electrophysiological tests in the ulnar and peroneal nerves, sympathetic skin responses from the palm and foot, and quantitative sensation testing from dermatomes C8 and S1. Discussion: The results of standard conduction tests of all nerves significantly differed between groups. The latency of sympathetic skin responses achieved from the foot was also statistically significantly prolonged in the study group. Significant differences were seen in both C8 and S1 regions for temperature and pain thresholds, and for vibratory threshold only in the S1 region, while the dispersions of low and high temperatures were important exclusively in the C8 region. Conclusions: We can conclude that co-exposure to many heavy metals results in explicit impairment of peripheral nerves. The lesion is more pronounced within small fibers and is predominantly connected with greater impairment of temperature-dependent pain thresholds. The evaluation of small fiber function should be considered in the early diagnosis of toxic polyneuropathy or in low-dose exposure to heavy metals.

Authors: Magdalena Koszewicz, Katarzyna Markowska, Marta Waliszewska-Prosol, Rafał Poreba, Paweł Gac, Anna Szymanska-Chabowska, Grzegorz

**Background: Chronic exposure to heavy metals affects various organs, among them the brain and peripheral nerves.**



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Mazur, Malgorzata Wieczorek, Maria Ejma, Krzysztof Slotwinski, Slawomir Budrewicz

Full Source: Journal of occupational medicine and toxicology (London, England) 2021 Apr 15;16(1):12. doi: 10.1186/s12995-021-00302-6.

### PHARMACEUTICAL/TOXICOLOGY

#### Fluorine-Specific Detection Using ICP-MS Helps to Identify PFAS Degradation Products in Nontargeted Analysis

2021-04-13

Although several per- and polyfluoroalkyl substances (PFAS) have been banned and classified as substances of very high concern by the European Chemicals Agency, similar chemicals remain widely used compounds to date. Even though more than 4700 PFASs may occur in the environment, only 40-50 compounds are routinely determined in targeted analysis by ESI-MS using isotopically labeled standards. Nontargeted analysis using high resolution (HR) molecular mass spectrometry suffers from a lack of data mining algorithms for identification and often low ionization efficiency of the compounds. An additional problem for quantification is the potential lack of suitable species specific standards. Here, we demonstrate the usefulness of a hard ionization source (ICP-MS/MS) as a fluorine-specific detector in combination with ESI-MS for the identification of fluorine containing compounds. Simultaneous hyphenation of HPLC-ICP-MS/MS with HR-ESI-MS is applied to evaluate biodegradation products of organofluorine compounds by sewage sludge. The data are analyzed in a nontarget approach using MZmine. Due to the fluorine-specific detection by ICP-MS/MS, more than 5000 peaks (features) of the ESI-MS were reduced to 15 features. Of these, one was identified as a PFAS degradation compound of fluorotelomer alcohol (8:2 FTOH) without using targeted analysis. The feasibility of the detection of organofluorine metabolites using a fluorine-specific detection was demonstrated using a model compound and can thus be applied to new experiments and unknown organofluorine containing samples in the future.

Authors: Steffen Heuckeroth, Tengetile N Nxumalo, Andrea Raab, Joerg Feldmann

Full Source: Analytical chemistry 2021 Apr 13. doi: 10.1021/acs.analchem.1c00031.

Although several per- and polyfluoroalkyl substances (PFAS) have been banned and classified as substances of very high concern by the European Chemicals Agency, similar chemicals remain widely used compounds to date.