

Bulletin Board

Contents

SEP. 03, 2021

[click on page numbers for links]

CHEMICAL EFFECTS

Endocrine disrupting chemicals (EDCs) and the neuroendocrine system: Beyond estrogen, androgen, and thyroid	3
Exposure to endocrine disrupting chemicals (EDCs) and cardiometabolic indices during pregnancy: The HOME Study	3
Endocrine-Disrupting Chemicals and Disorders of Penile Development in Humans.....	4

ENVIRONMENTAL RESEARCH

A critical synthesis of current peer-reviewed literature on the environmental and human health impacts of COVID-19 PPE litter: New findings and next steps	5
The environmental impacts of citrus residue management in China: A case study in The Three Gorges Reservoir Region	6

OCCUPATIONAL

Occupational exposure to gasoline in gasoline station male attendants promotes M1 polarization in macrophages	6
Construction and Calibration of an Exposure Matrix for the Welding Trades.....	7
Chemical contaminant exposures assessed using silicone wristbands among occupants in office buildings in the USA, UK, China, and India	9
Occupational hand dermatitis web survey in a university hospital during COVID-19 pandemic: the SHIELD study.....	10

PHARMACEUTICAL/TOXICOLOGY

Urinary phthalate metabolites mixture, serum cytokines and renal function in children: A panel study.....	10
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Bulletin Board

Technical

SEP. 03, 2021

CHEMICAL EFFECTS

Endocrine disrupting chemicals (EDCs) and the neuroendocrine system: Beyond estrogen, androgen, and thyroid

2021

Hundreds of anthropogenic chemicals occupy our bodies, a situation that threatens the health of present and future generations. This chapter focuses on endocrine disrupting compounds (EDCs), both naturally occurring and man-made, that affect the neuroendocrine system to adversely impact health, with an emphasis on reproductive and metabolic pathways. The neuroendocrine system is highly sexually dimorphic and essential for maintaining homeostasis and appropriately responding to the environment. Comprising both neural and endocrine components, the neuroendocrine system is hormone sensitive throughout life and touches every organ system in the body. The integrative nature of the neuroendocrine system means that EDCs can have multi-system effects. Additionally, because gonadal hormones are essential for the sex-specific organization of numerous neuroendocrine pathways, endocrine disruption of this programming can lead to permanent deficits. Included in this review is a brief history of the neuroendocrine disruption field and a thorough discussion of the most common and less well understood neuroendocrine disruption modes of action. Also provided are extensive examples of how EDCs are likely contributing to neuroendocrine disorders such as obesity, and evidence that they have the potential for multi-generational effects.

Authors: Heather B Patisaul

Full Source: *Advances in pharmacology* (San Diego, Calif.) 2021;92:101-150. doi: 10.1016/bs.apha.2021.03.007.**Exposure to endocrine disrupting chemicals (EDCs) and cardiometabolic indices during pregnancy: The HOME Study**

2021-11

Background: Toxicology studies have identified pregnancy as a window of susceptibility for endocrine disrupting chemicals (EDCs) and cardiometabolic indices in women. No study in humans, however, has examined EDC mixtures and cardiometabolic indices during pregnancy. Methods: We used the Health Outcomes and Measures of the Environment (HOME) Study to examine whether bisphenol A (BPA), polybrominated diphenyl ethers (PBDEs), per- and polyfluoroalkyl

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Bulletin Board

Technical

SEP. 03, 2021

substances (PFAS), and phthalates are associated with blood pressure, glucose, and lipids in 388 pregnant women. We measured PBDEs and PFAS in serum at 16 weeks gestation, while BPA and phthalate metabolites were quantified in urine at 16 and 26 weeks gestation. We used linear regression and Bayesian Kernel Machine Regression (BKMR) to estimate covariate-adjusted associations of individual EDCs and their mixtures with cardiometabolic indices during pregnancy. Results: A 10-fold increase in BDE-28 was associated with a 13.1 mg/dL increase in glucose [95% Confidence Interval (CI) 2.9, 23.2] in linear regression. The BKMR model also identified BDE-28 as having a positive association with glucose. BDE-28, BDE-47, and BDE-99 were positively associated with total cholesterol in both single- and multi-pollutant models, whereas a suggestive negative association was noted with BDE-153. Mono-n-butyl phthalate (MBP) ($\beta = -7.9$ mg/dL, 95% CI -12.9, -3.0) and monobenzyl phthalate (MBzP) ($\beta = -6.3$ mg/dL, 95% CI -10.6, -2.0) were both associated with significant decreases in cholesterol in linear regression, but only MBzP was identified as an important contributor in the BKMR model.

Conclusion: Overall, we observed positive associations between PBDEs with glucose and cholesterol levels during pregnancy, while negative associations were found between some phthalate biomarkers and cholesterol. No relationship was noted for BPA or PFAS with cardiometabolic indices during pregnancy across both models.

Authors: Ann M Vuong, Joseph M Braun, Andreas Sjödin, Antonia M Calafat, Kimberly Yolton, Bruce P Lanphear, Aimin Chen

Full Source: *Environment international* 2021 Nov;156:106747. doi: 10.1016/j.envint.2021.106747.**Endocrine-Disrupting Chemicals and Disorders of Penile Development in Humans**

2021-08-26

This paper reviews the current knowledge on the environmental effects on penile development in humans. The specific focus is on endocrine-disrupting chemicals (EDCs), a heterogeneous group of natural or manmade substances that interfere with endocrine function, and whether they can induce hypospadias and micropenis in male neonates. Epidemiological data and animal observations first raised suspicions about environmental effects, leading to the testis dysgenesis syndrome (TDS) hypothesis. More recent research has provided stronger indications that TDS may indeed be the result of the direct or indirect effects of EDCs. Drawing on epidemiological and toxicological studies, we also report on

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Bulletin Board

Technical

SEP. 03, 2021

the effects of maternal diet and substances like pesticides, phthalates, bisphenol A, and polychlorinated biphenyls. Proximity to contamination hazards and occupational exposure are also suspected to contribute to the occurrence of hypospadias and micropenis. Lastly, the cumulative effects of EDCs and the possibility of transgenerational effects, with the penile development of subsequent generations being affected, raise concerns for long-term public health.

Authors: Laura Gaspari, Benoit Tessier, Françoise Paris, Anne Bergougnoux, Samir Hamamah, Charles Sultan, Nicolas Kalfa

Full Source: Sexual development : genetics, molecular biology, evolution, endocrinology, embryology, and pathology of sex determination and differentiation 2021 Aug 26;1-16. doi: 10.1159/000517157.

ENVIRONMENTAL RESEARCH

A critical synthesis of current peer-reviewed literature on the environmental and human health impacts of COVID-19 PPE litter: New findings and next steps

2021-08-18

Since the emergence of Coronavirus disease (COVID-19), the threat of plastic waste pollution has grown exponentially, with a strong attention on the environmental and human health consequences of millions of personal protective equipment (PPE) (e.g., face masks, shields, gloves, and wipes) being used and discarded. In response, a massive research effort has been launched to understand, characterize, and estimate the exposure risks of PPE associated contaminants. While the number of studies examining the impacts of PPE is increasing, this review aimed to provide a quick update on the research conducted to date of this topic, as well as to identify priorities for future research. Specifically, we analyzed recent global peer-reviewed articles on PPE to synthesize methods, control measures, and documented evidence to (1) investigate the discarded PPE in a variety of environments; (2) determine the microplastics discharge in the aquatic environment; (3) examine the intentionally or unintentionally added chemicals in the production of PPE; and (4) assess potential human health hazards and exposure pathways. Despite progress, more research is needed in the future to fully understand the chemical emissions from PPE

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Bulletin Board

Technical

SEP. 03, 2021

degradation mechanisms (mechanical, chemical, and biological), as well as the magnitude and density of PPE pollution in the environment.

Authors: Gurusamy Kutralam-Muniasamy, Fermín Pérez-Guevara, V C Shruti

Full Source: Journal of hazardous materials 2021 Aug 18;422:126945. doi: 10.1016/j.jhazmat.2021.126945.

The environmental impacts of citrus residue management in China: A case study in The Three Gorges Reservoir Region

2021-09

This study conducted the first life cycle analysis for citrus residue (CR) management systems in China. The results indicated conventional waste treatment systems were not suitable for CR management in China. Although feed system seems to be a favourable option, the uncertainty analysis suggested valorisation system could achieved better performance in global warming, eutrophication and human toxicity. The environmental impacts of valorisation systems were more sensitive to energy consumption. For silage and single cell protein (SCP) system, the environmental impacts could be significantly reduced by improving the energy use efficiency or using more renewable energy. In comparison, although the environmental impacts of biorefinery system were less favourable than SCP and silage systems. The multiple extraction unit had less impact than reported values in other studies. Further research in biorefinery system can focus on increasing the energy efficiency of pre-treatment or reuse of extraction chemicals.

Authors: Wenhao Chen, Yueming Zhou, Youpeng Chen

Full Source: Waste management (New York, N.Y.) 2021 Sep;133:80-88. doi: 10.1016/j.wasman.2021.07.037.

This study conducted the first life cycle analysis for citrus residue (CR) management systems in China.

OCCUPATIONAL

Occupational exposure to gasoline in gasoline station male attendants promotes M1 polarization in macrophages

2021-08-27

Several studies have reported the toxicological implications of exposure to petroleum hydrocarbon fumes in animal models. There is little documentation on the effect of such exposure on oxidative stress levels and immune response. To our knowledge, no documentation of

Bulletin Board

Technical

SEP. 03, 2021

M1 polarization in macrophages in gasoline station male attendants. Therefore, this study aimed to evaluate the harmful effects of gasoline vapors in 62 male attendants (16-70 years) compared to 29 age- and sex-matched-unexposed controls. The attendants were recruited from Damietta governorate gasoline stations. Gasoline exposure induced a significant increase in tumor necrosis factor- α (TNF- α) level ($p < 0.05$) as well as a slight but non-significant increase in the activity of acidic mammalian chitinase (AMCase) ($p > 0.05$). Further TNF- α /AMCase ratio was significantly increased ($p < 0.01$) in sera of the attendants when compared to those of the healthy controls. Also, the total leucocytic and lymphocytic counts were significantly increased ($p < 0.01$ and $p < 0.001$, respectively). On contrary, neutrophils to lymphocytes ratio (NLR) and platelets to lymphocytes ratio (PLR) were significantly decreased ($p < 0.05$ and $p < 0.001$, respectively). In addition, significant reduction in hemoglobin (Hb) concentration, plasma glutathione reduced form (GSH), and catalase, as well as superoxide dismutase (SOD) activities in red blood cells were observed in the exposed attendants. As a result, malondialdehyde (MDA), nitric oxide (NO) levels, and NO/AMCase ratio were significantly increased ($p < 0.05$). In conclusion, this study inferred that prolonged gasoline exposure can mediate immune activation, especially M1 macrophages polarization, possibly via oxidative stress-mediated mechanism.

Authors: El-Shahat A Toson, Entsar A Saad, Hadeer Abd El-Raouf Omar
Full Source: Environmental science and pollution research international 2021 Aug 27. doi: 10.1007/s11356-021-16019-2.

Construction and Calibration of an Exposure Matrix for the Welding Trades

2021-08-28

Objectives: This study aimed to construct, validate, and calibrate an exposure matrix that would be used to estimate personal airborne exposures to total dust, manganese, nickel, chromium, and aluminum for welders in the WHAT-ME cohort. The Workers' Health in Apprenticeship Trades: metal and electrical (WHAT-ME) study established a cohort of women and men welders to investigate pregnancy and other birth outcomes along with health issues related to welding. To construct the matrix, data were extracted and assembled from the literature and analyzed to produce exposure models. Final models derived in this first step were then compared with external data gathered under controlled conditions and later combined to form calibrated models.

Methods: A systematic literature search was conducted to identify and extract all relevant data from published journal articles appearing in

Objectives: This study aimed to construct, validate, and calibrate an exposure matrix that would be used to estimate personal airborne exposures to total dust, manganese, nickel, chromium, and aluminum for welders in the WHAT-ME cohort.

Bulletin Board

Technical

SEP. 03, 2021

selected databases. Summary data were extracted that represented airborne personal exposures to total, inhalable and respirable dusts along with metal concentrations for manganese, nickel, chromium, and aluminum. Mathematical exposure models were derived and a validation of the models undertaken in the second part of this study. The most common welding combinations of welding process, base metal, and consumable (welding scenarios) for welders taking part in the WHAT-ME study were identified through detailed welding questionnaires completed by WHAT-ME participants. These were replicated under controlled conditions with a welder equipped with a personal air sampling pump to gather samples. A gravimetric analysis was performed to determine total dust exposures followed by a metals analysis using ICP-MS. Predictions were made for these welding scenarios replicated in the laboratory, using the exposure models derived in the literature and the predictions correlated against the results from the welding laboratory replications.

Results: The systematic review yielded 92 published articles from which 737 summary statistics were extracted representing 4620 personal samples of total dust, 4762 of manganese, 4679 of nickel, 3972 of chromium, and 676 of aluminum. The highest total dust exposures were for flux-core arc welding (FCAW) while the highest manganese producing base metal was mild steel. For nickel, the highest emissions were from high alloyed steel using gas metal arc welding while chromium emissions were most abundant in manual metal arc welding on stainless steel. Aluminum exposures were highest in FCAW welding and on aluminum as a base metal. The replication of 21 scenarios covered more than 90% of the scenarios in the WHAT-ME study. Sixty-one laboratory welding sessions took place with a minimum of two replications per scenario. Spearman rank correlations between predicted exposures and mean measured exposures yielded a rho of 0.93 ($P < 0.001$) for total dust, 0.87 ($P < 0.001$) for manganese, 0.54 ($P < 0.024$) for nickel, 0.43 ($P = 0.055$) for chromium, and 0.29 ($P = 0.210$) for aluminum.

Conclusions: This study produced the first welding exposure matrix composed of process, base metal, and consumable. This model was able to predict exposures observed under controlled conditions and could be used by any researcher to estimate welding exposures in a wide range of occupational contexts.

Authors: Jean-Michel Galarneau

Full Source: Annals of work exposures and health 2021 Aug 28;wxab071. doi: 10.1093/annweh/wxab071.

Bulletin Board

Technical

SEP. 03, 2021

Chemical contaminant exposures assessed using silicone wristbands among occupants in office buildings in the USA, UK, China, and India

2021-11

Little is known about chemical contaminant exposures of office workers in buildings globally. Complex mixtures of harmful chemicals accumulate indoors from building materials, building maintenance, personal products, and outdoor pollution. We evaluated exposures to 99 chemicals in urban office buildings in the USA, UK, China, and India using silicone wristbands worn by 251 participants while they were at work. Here, we report concentrations of polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) and other brominated flame retardants (BFRs), organophosphate esters (OPEs), phthalates and phthalate alternatives, pesticides, and polycyclic aromatic hydrocarbons (PAHs). First, we found major differences in office worker chemical exposures by country, some of which can be explained by regulations and use patterns. For example, exposures to several pesticides were substantially higher in India where there were fewer restrictions and unique malaria challenges, and exposures to flame retardants tended to be higher in the USA and UK where there were historic, stringent furniture flammability standards. Higher exposures to PAHs in China and India could be due to high levels of outdoor air pollution that penetrates indoors. Second, some office workers were still exposed to legacy PCBs, PBDEs, and pesticides, even decades after bans or phase-outs. Third, we identified exposure to a contemporary PCB that is not covered under legacy PCB bans due to its presence as an unintentional byproduct in materials. Fourth, exposures to novel BFRs, OPEs, and other chemicals commonly used as substitutes to previously phased-out chemicals were ubiquitous. Fifth, some exposures were influenced by individual factors, not just countries and buildings. Phthalate exposures, for example, were related to personal care product use, country restrictions, and building materials. Overall, we found substantial country differences in chemical exposures and continued exposures to legacy phased-out chemicals and their substitutes in buildings. These findings warrant further research on the role of chemicals in office buildings on worker health.

Authors: Anna S Young, Nicholas Herkert, Heather M Stapleton, Jose Guillermo Cedeño Laurent, Emily R Jones, Piers MacNaughton, Brent A Coull, Tamarra James-Todd, Russ Hauser, Marianne Lahaie Luna, Yu Shan Chung, Joseph G Allen

Full Source: Environment international 2021 Nov;156:106727. doi: 10.1016/j.envint.2021.106727.

Little is known about chemical contaminant exposures of office workers in buildings globally.

Bulletin Board

Technical

SEP. 03, 2021

Occupational hand dermatitis web survey in a university hospital during COVID-19 pandemic: the SHIELD study

2021-08-26

Background: Occupational hand dermatitis (OHD) is a skin disease occurring on employees' hands in certain jobs. Little is known about prevalence, incidence and characteristics of this adverse skin reaction and its associated risk factors during COVID-19 pandemic. To evaluate both prevalence and incidence of OHD and associated risk factors in Italian clinicians. Methods: A cross-sectional study was performed using a self-report questionnaire. Results: Two hundred and thirty clinicians responded to the survey and 82% of responders did not report previous OHD history before the COVID-19 pandemic. Daily use of gloves was reported by 80% of responders. OHD prevalence was 18%, while incidence was 80%. We found a protective effect on symptom occurrence for vinyl/nitrile gloves if the time with gloves was ≥ 6 hours per day. Conclusions: This survey reveals a high OHD incidence in an Italian population of clinicians. Furthermore, wearing vinyl/nitrile gloves for at least 6 hours a day had a protective effect on symptom onset.

Authors: Angela Rizzi, Riccardo Inchingolo, Marinella Viola, Luca Boldrini, Jacopo Lenkowitz, Franziska Michaela Lohmeyer, Francesco Maria De Simone, Domenico Staiti, Caterina Sarnari, Antonio Gasbarrini, Eleonora Nucera

Full Source: La Medicina del lavoro 2021 Aug 26;112(4):320-326. doi: 10.23749/mdl.v112i4.11670.

Background: Occupational hand dermatitis (OHD) is a skin disease occurring on employees' hands in certain jobs.

PHARMACEUTICAL/TOXICOLOGY**Urinary phthalate metabolites mixture, serum cytokines and renal function in children: A panel study**

2021-08-20

Epidemiological evidence regarded the relations of phthalates with children's renal function and its underlying mechanism were largely unknown. We conducted a panel study using 287 paired urine-blood samples by repeated measurements of 103 children (4-13 years) across 3 seasons to explore effects of urinary phthalate metabolites on estimated glomerular filtration rate (eGFR) and the potential role of multiple cytokines. We found that mono-ethyl phthalate (MEP), monobutyl phthalate (MBP), mono-benzyl phthalate (MBzP) and mono-n-octyl phthalate (MOP) were significantly associated with eGFR reduction. Compared with the lowest quartile, MBP, MBzP and MEP in the third and fourth quartiles exhibited a

Bulletin Board

Technical

SEP. 03, 2021

graded decrease in eGFR. Meanwhile, weighted quantile sum regression analyses showed an inverse association of metabolites mixture with eGFR, to which MEP, MBzP, MOP were the major contributors. MEP also remained robust in multiple-phthalate model. Age and weight status might modify such relationships with significant interactions. Furthermore, eGFR related phthalate metabolites were associated with increased multiple cytokines, and CCL27, CXCL1 might be potential mediators between MEP and eGFR with mild mediated proportions. Accordingly, urinary phthalate metabolites were related to eGFR reduction in dose-response manner and multiple cytokines elevation, of which CCL27 and CXCL1 might partly mediate phthalate-associated decreased renal function among children.

Authors: Miao Liu, Lei Zhao, Linlin Liu, Wenting Guo, Huihua Yang, Shuang Chen, Jie Yu, Meng Li, Qin Fang, Xuefeng Lai, Liangle Yang, Rui Zhu, Xiaomin Zhang

Full Source: Journal of hazardous materials 2021 Aug 20;422:126963.
doi: 10.1016/j.jhazmat.2021.126963.