

# Bulletin Board

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## Bulletin Board

## Technical

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## CHEMICAL EFFECTS

**Persistent organic pollutants in foods, their interplay with gut microbiota and resultant toxicity**

2022-04-05

Persistent Organic Pollutants (POPs) have become immensely prevalent in the environment as a result of their unique chemical properties (persistent, semi-volatile and bioaccumulative nature). Their occurrence in the soil, water and subsequently in food has become a matter of concern. With food being one of the major sources of exposure, the detrimental impact of these chemicals on the gut microbiome is inevitable. The gut microbiome is considered as an important integrant for human health. It participates in various physiological, biochemical and immunological activities; thus, affects the metabolism and physiology of the host. A myriad of studies have corroborated an association between POP-induced gut microbial dysbiosis and prevalence of disorders. For instance, ingestion of polychlorinated biphenyls, polybrominated diphenyl ethers or organochlorine pesticides influenced bile acid metabolism via alteration of bile salt hydrolase activity of *Lactobacillus*, *Clostridium* or *Bacteroides* genus. At the same time, some chemicals such as DDE have the potential to elevate Proteobacteria and Firmicutes/Bacteroidetes ratio influencing their metabolic activity leading to enhanced short-chain fatty acid synthesis, ensuing obesity or a pre-diabetic state. This review highlights the impact of POPs exposure on the gut microbiota composition and metabolic activity, along with an account of its corresponding consequences on the host physiology. The critical role of gut microbiota in impeding the POPs excretion out of the body resulting in their prolonged exposure and consequently, enhanced degree of toxicity is also emphasized.

Authors: Shivani Popli, Prarabdh C Badgujar, Tripti Agarwal, Bharat Bhushan, Vijendra Mishra

Full Source: The Science of the total environment 2022 Apr 5;155084. doi: 10.1016/j.scitotenv.2022.155084.

**Ocean acidification alters sperm responses to egg-derived chemicals in a broadcast spawning mussel**

2022-04

The continued emissions of anthropogenic carbon dioxide are causing progressive ocean acidification (OA). While deleterious effects of OA on biological systems are well documented in the growth of calcifying

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organisms, lesser studied impacts of OA include potential effects on gamete interactions that determine fertilization, which are likely to influence the many marine species that spawn gametes externally. Here, we explore the effects of OA on the signalling mechanisms that enable sperm to track egg-derived chemicals (sperm chemotaxis). We focus on the mussel *Mytilus galloprovincialis*, where sperm chemotaxis enables eggs to bias fertilization in favour of genetically compatible males. Using an experimental design based on the North Carolina II factorial breeding design, we test whether the experimental manipulation of seawater pH (comparing ambient conditions to predicted end-of-century scenarios) alters patterns of differential sperm chemotaxis. While we find no evidence that male-female gametic compatibility is impacted by OA, we do find that individual males exhibit consistent variation in how their sperm perform in lowered pH levels. This finding of individual variability in the capacity of ejaculates to respond to chemoattractants under acidified conditions suggests that climate change will exert considerable pressure on male genotypes that can withstand an increasingly hostile fertilization environment.

Authors: Rowan A Lymbery, Jill Brouwer, Jonathan P Evans

Full Source: Biology letters 2022 Apr;18(4):20220042. doi: 10.1098/rsbl.2022.0042.

## ENVIRONMENTAL RESEARCH

**Autism-like symptoms by exposure to air pollution and valproic acid-induced in male rats**

2022-04-06

Exposure to air pollution during prenatal or neonatal periods is associated with autism spectrum disorder (ASD) according to epidemiology studies. Furthermore, prenatal exposure to valproic acid (VPA) has also been found to be associated with an increased prevalence of ASD. To assess the association between simultaneous exposure to VPA and air pollutants, seven exposure groups of rats were included in current study (PM2.5 and gaseous pollutants exposed - high dose of VPA (PGE-high); PM2.5 and gaseous pollutants exposed - low dose of VPA (PGE-low); gaseous pollutants only exposed - high dose of VPA (GE-high); gaseous pollutants only exposed - low dose of VPA (GE-low); clean air exposed - high dose of VPA (CAE-high); clean air exposed - low dose of VPA (CAE-low) and clean air exposed (CAE)). The pollution-exposed rats were exposed to air pollutants from embryonic day (E0) to postnatal day 42 (PND42). In all the induced groups, decreased oxidative stress biomarkers, decreased oxytocin

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receptor (OXTR) levels, and increased the expression of interleukin 6 (IL-6), interleukin 1 $\beta$  (IL-1 $\beta$ ), and tumor necrosis factor alpha (TNF- $\alpha$ ) were found. The volumes of the cerebellum, hippocampus, striatum, and prefrontal decreased in all induced groups in comparison to CAE. Additionally, increased numerical density of glial cells and decreased of numerical density of neurons were found in all induced groups. Results show that simultaneous exposure to air pollution and VPA can cause ASD-related behavioral deficits and air pollution reinforced the mechanism of inducing ASD s in VPA-induced rat model of autism.

Authors: Bahran Imam, Masoumeh Rahmatinia, Abbas Shahsavani, Fariba Khodagholi, Philip K Hopke, Shahriyar Bazazzpour, Mostafa Hadei, Maryam Yarahmadi, Mohammad-Amin Abdollahifar, Mehdi Amouei Torkmahalleh, Majid Kermani, Saba Ilkhani, Seyed Hamidreza MirBehbahani

Full Source: Environmental science and pollution research international 2022 Apr 6. doi: 10.1007/s11356-022-19865-w.

### Research on COVID-19 and air pollution: A path towards advancing exposure science

2022-04-04

The COVID-19 pandemic has resulted in an extraordinary incidence of morbidity and mortality, with almost 6 million deaths worldwide at the time of this writing (<https://covid19.who.int/>). There has been a pressing need for research that would shed light on factors - especially modifiable factors - that could reduce risks to human health. At least several hundred studies addressing the complex relationships among transmission of SARS-CoV-2, air pollution, and human health have been published. However, these investigations are limited by available and consistent data. The project goal was to seek input into opportunities to improve and fund exposure research on the confluence of air pollution and infectious agents such as SARS-CoV-2. Thirty-two scientists with expertise in exposure science, epidemiology, risk assessment, infectious diseases, and/or air pollution responded to the outreach for information. Most of the respondents expressed value in developing a set of common definitions regarding the extent and type of public health lockdown. Traffic and smoking ranked high as important sources of air pollution warranting source-specific research (in contrast with assessing overall ambient level exposures). Numerous important socioeconomic factors were also identified. Participants offered a wide array of inputs on what they considered to be essential studies to improve our understanding of exposures. These ranged from detailed mechanistic studies to improved air quality monitoring studies and prospective cohort studies. Overall,

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many respondents indicated that these issues require more research and better study design. As an exercise to solicit opinions, important concepts were brought forth that provide opportunities for scientific collaboration and for consideration for funding prioritization. Further conversations on these concepts are needed to advance our thinking on how to design research that moves us past the documented limitations in the current body of research and prepares us for the next pandemic.

Authors: Carol J Burns, Judy S LaKind, Josh Naiman, Denali Boon, Jane Ellen Clougherty, Ana M Rule, Angelika Zidek

Full Source: Environmental research 2022 Apr 4;113240. doi: 10.1016/j.envres.2022.113240.

### PHARMACEUTICAL/TOXICOLOGY

#### Perfluoroalkyl substance mixtures and cardio-metabolic outcomes in highly exposed male workers in the Veneto Region: A mixture-based approach

2022-04-04

**Background:** Perfluoroalkyl substances (PFAS) have been consistently associated with cardio-metabolic traits. Occupational exposures to multiple PFAS with health outcomes have been poorly investigated. The aim of the present study was to examine these associations among former workers involved in PFAS production.

**Methods:** We considered 232 male ex-employees who had worked in a factory (Trissino, Veneto Region, Italy), which produced PFAS and other chemicals during 1968-2018. Out of twelve serum PFAS, only four (PFOA, PFOS, PFHxS, and PFNA) were quantifiable in at least 50% of samples. Non-fasting serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured. The associations between serum PFAS mixture and considered outcomes were assessed through linear regression mixed models and Weighted Quantile Sum (WQS) regression, adjusting for potential confounders.

**Results:** PFOA was detected at the highest level, with a median concentration (in ng/mL) of 80.8 (min-max: 0.35-13,033), followed by PFOS (median: 8.55, min-max: 0.35-343), PFHxS (median: 6.8, min-max: 0.35-597) and PFNA (median: 0.8, min-max: 0.35-5). We observed that each A quartile increase in the WQS index was positively associated with the levels of TC ( $\beta$ : 8.41, 95% IC: 0.78-16.0), LDL-C ( $\beta$ : 8.02, 95% IC: 1-15.0) and SBP ( $\beta$ : 3.21, 95% IC: 0.82-5.60). No association of serum PFAS concentration on HDL

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cholesterol and DBP emerged. WQS analyses revealed a major contribution of PFNA and PFHxS for the cholesterol levels, although PFOA reported the highest concentration. PFOA and PFOS emerged as chemicals of concern regarding the association with SBP. Conclusions: The results showed a clear association between serum PFAS levels and markers of cardiovascular risk and support the importance of clinical surveillance of cardiovascular risk factors in population with a high exposure to PFAS, especially in the occupational setting.

Authors: Erich Batzella, Paolo Girardi, Francesca Russo, Gisella Pitter, Filippo Da Re, Tony Fletcher, Cristina Canova

Full Source: Environmental research 2022 Apr 4;212(Pt A):113225. doi: 10.1016/j.envres.2022.113225.

### Review of Inhalation Health Risks Involving Chloromethylisothiazolinone (CMIT) and Methylisothiazolinone (MIT) Used as Disinfectants in Household Humidifiers

2022-04-04

The association between lung injury and exposure to humidifier disinfectant (HD) containing a mixture of chloromethylisothiazolinone (CMIT) and methylisothiazolinone (MIT) has been controversial in South Korea. This study conducts a literature review in order to evaluate the likelihood of CMIT/MIT reaching the lower part of the respiratory tract and causing lung injury. A literature review focused on the inhalation risk of HD containing a mixture of CMIT and MIT. The major contents included the physicochemical properties of CMIT and MIT contained in HDs and methodological reviews on substance analysis, toxicity tests and clinical cases. HD products marketed in South Korea have been reported to contain approximately 1-2% CMIT and 0.2-0.6% MIT along with magnesium nitrate (20-25%), magnesium chloride (0.2-1.0%), and water (70-75%). The types of CMIT and MIT dispersed into the air and deposited in the respiratory tract are assumed to be either gaseous substances or nanoparticles mixed with magnesium salts. The result of the literature review including clinical cases of lung injury among CMIT/MIT HD product users, demonstrated that these chemicals likely reach the lower respiratory tract and accordingly cause lung injury. A number of humidifier disinfectant-associated lung injury cases with clinical evidence should be prioritized in risk assessment of HD containing CMIT and MIT, even though there might be insufficient evidence in all related areas,

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including inhalation exposure assessment studies, animal testing, and epidemiological studies.

Authors: Jiwon Kim, Soyoung Park, Kyung Ehi Zoh, Jihoon Park, Sangjun Choi, Sung Ho Hwang, So-Yeon Lee, Dong-Uk Park

Full Source: Journal of Korean medical science 2022 Apr 4;37(13):e101. doi: 10.3346/jkms.2022.37.e101.

## OCCUPATIONAL

### Dose-response relationship of pulmonary disorders by inhalation exposure to cross-linked water-soluble acrylic acid polymers in F344 rats

2022-04-08

Background: In Japan, six workers handling cross-linked water-soluble acrylic acid polymer (CWAAP) at a chemical plant suffered from lung diseases, including fibrosis, interstitial pneumonia, emphysema, and pneumothorax. We recently demonstrated that inhalation of CWAAP-A, one type of CWAAP, causes pulmonary disorders in rats. It is important to investigate dose-response relationships and recoverability from exposure to CWAAPs for establishing occupational health guidelines, such as setting threshold limit value for CWAAPs in the workplace.

Methods: Male and female F344 rats were exposed to 0.3, 1, 3, or 10 mg/m<sup>3</sup> CWAAP-A for 6 h/day, 5 days/week for 13 weeks using a whole-body inhalation exposure system. At 1 h, 4 weeks, and 13 weeks after the last exposure the rats were euthanized and blood, bronchoalveolar lavage fluid, and all tissues including lungs and mediastinal lymph nodes were collected and subjected to biological and histopathological analyses. In a second experiment, male rats were pre-treated with clodronate liposome or polymorphonuclear leukocyte-neutralizing antibody to deplete macrophages or neutrophils, respectively, and exposed to CWAAP-A for 6 h/day for 2 days. Results: CWAAP-A exposure damaged only the alveoli. The lowest observed adverse effect concentration (LOAEC) was 1 mg/m<sup>3</sup> and the no observed adverse effect concentration (NOAEC) was 0.3 mg/m<sup>3</sup>. Rats of both sexes were able to recover from the tissue damage caused by 13 weeks exposure to 1 mg/m<sup>3</sup> CWAAP-A. In contrast, tissue damage caused by exposure to 3 and 10 mg/m<sup>3</sup> was irreversible due to the development of interstitial lung lesions. There was a gender difference in the recovery from CWAAP-A induced pulmonary disorders, with females recovering less than males. Finally, acute lung effects caused by CWAAP-A were significantly reduced by depletion of alveolar

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macrophages. **Conclusions:** Pulmonary damage caused by inhalation exposure to CWAAP-A was dose-dependent, specific to the lung and lymph nodes, and acute lung damage was ameliorated by depleting macrophages in the lungs. CWAAP-A had both a LOAEC and a NOAEC, and tissue damage caused by exposure to 1 mg/m<sup>3</sup> CWAAP-A was reversible: recovery in female rats was less than for males. These findings indicate that concentration limits for CWAAPs in the workplace can be determined.

**Authors:** Tomoki Takeda, Shotaro Yamano, Yuko Goto, Shigeyuki Hirai, Yusuke Furukawa, Yoshinori Kikuchi, Kyohei Misumi, Masaaki Suzuki, Kenji Takanobu, Hideki Senoh, Misae Saito, Hitomi Kondo, George Daghljan, Young-Kwon Hong, Yasuhiro Yoshimatsu, Masanori Hirashima, Yoichiro Kobashi, Kenzo Okamoto, Takumi Kishimoto, Yumi Umeda  
**Full Source:** Particle and fibre toxicology 2022 Apr 8;19(1):27. doi: 10.1186/s12989-022-00468-9.

### Maternal occupational exposures and fetal growth in a Spanish birth cohort

2022-04-07

While the epidemiologic literature suggests certain maternal occupational exposures may be associated with reduced measures of size at birth, the occupational literature employing fetal biometry data to assess fetal growth is sparse. The present study examines associations between maternal occupational exposures and ultrasound-measured fetal growth. We included 1,739 singleton pregnancies from the INfancia y Medio Ambiente (INMA) project (2003-2008). At 32 weeks of pregnancy, interviewers ascertained mothers' employment status and assessed job-related physical loads, work schedules, and job strain during pregnancy. Job titles were linked to a job-exposure matrix to estimate exposure to 10 endocrine disrupting chemical (EDC) groups. We calculated z-scores from longitudinal growth curves representing trajectories from 0-12, 12-20 and 20-34 gestational weeks for abdominal circumference (AC), biparietal diameter (BPD), femur length (FL), and estimated fetal weight (EFW). Linear mixed models clustered by IMNA region (i.e., Gipuzkoa, Sabadell, Valencia) were used to examine associations between occupational exposures and fetal growth. Effect estimates are presented as percentage change in fetal growth. There was limited evidence of associations between work-related non-chemical stressors and fetal growth. We observed associations of similar magnitude between multiple EDC groups and decreased EFW trajectories during 20-34 gestational weeks (phthalates: -1.4% [-3.5, 0.6%]; alkylphenolic compounds (APCs): -1.1% [-2.3, 0.1%]; miscellaneous chemicals: -1.5% [-3.7, 0.8%]), while

While the epidemiologic literature suggests certain maternal occupational exposures may be associated with reduced measures of size at birth, the occupational literature employing fetal biometry data to assess fetal growth is sparse.

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miscellaneous chemicals were associated with increased BPD from 12-20 weeks (2.1% [0.8, 3.5%]). Notably, 67% of women exposed to phthalates were hairdressers; 68% of women exposed to APCs worked as domestic cleaners. In conclusion, we found limited evidence that maternal occupational exposures impact fetal growth. Further research should consider the combined impact of multiple workplace exposures.

**Authors:** Jennifer Ish, David Gimeno Ruiz de Porras, Elaine Symanski, Ferran Ballester, Maribel Casas, George L Delclos, Mònica Guxens, Jesús Ibarluzea, Carmen Iñiguez, Loreto Santa-Marina, Michael D Swartz, Kristina W Whitworth  
**Full Source:** PloS one 2022 Apr 7;17(4):e0264530. doi: 10.1371/journal.pone.0264530.

### A nationwide survey of 20 legacy brominated flame retardants in indoor dust from China: continuing occurrence, national distribution, and implication for human exposure

2022-04-04

Despite the restrictions on polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDDs), these chemicals are still ubiquitous environmental pollutants. In this study, we measured the concentrations and profiles of 17 PBDE congeners and 3 HBCDD isomers in indoor dust samples collected from 23 provinces and cities across China. The summed concentrations of PBDEs ( $\Sigma$ 17PBDEs) ranged from 4.19 to 817 ng/g, with an average of  $171 \pm 184$  ng/g. BDE-209 was the most abundant congener. The concentrations of HBCDDs ranged from 6.65 to 1335 ng/g, with an average of  $236 \pm 324$  ng/g. Unlike commercial HBCDD formulations,  $\alpha$ -HBCDD was the predominant isomer in the indoor dust samples analyzed. Geographical distributions showed that the concentrations of PBDEs and HBCDDs varied significantly among different regions. Higher PBDE and HBCDD levels were observed in samples from eastern coastal and economically developed regions. Further, we estimated the daily intakes of PBDEs and HBCDDs through the routes of dust ingestion and dust dermal absorption for different age groups. Dust dermal absorption is an unneglectable exposure pathway to PBDEs and HBCDDs for the Chinese population. Among the age groups, infants had the highest exposure via dust dermal absorption, and toddlers had the highest exposure via dust ingestion. Compared with the threshold values, the exposure doses of PBDEs and HBCDDs are unlikely to pose significant health concerns for

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both infants and adults in China. This is the first national survey of PBDEs and HBCDDs in indoor dust samples across China after the restriction.

Authors: Haifeng Li, Yuxian Liu, Yongyin Lan, Yanan Zhao, Anxiang Lu, Cheng Li, Rongrong Lei, Jingchuan Xue, Wenbin Liu

Full Source: Environmental science and pollution research international 2022 Apr 4. doi: 10.1007/s11356-022-19850-3.

### What should be tested in patients with suspected mold exposure? Usefulness of serological markers for the diagnosis

2022-03-29

The associations of mold exposure, IgE-mediated sensitization, inflammatory markers, and respiratory symptoms were analyzed in 46 exposed and 23 non-exposed individuals. Both exposure and clinical symptoms were assessed by questionnaire. Specific (s)IgE to mold mixture (mx1) was significantly higher and found more frequently in exposed (41%) than non-exposed individuals (17%), which was not observed for sIgG to mold mix (Gmx6). Notably, exposed asthmatics were more frequently sensitized to molds (55%) compared to exposed non-asthmatics (18%). In addition, the serum concentrations of club cell protein (CC16) were significantly lower in exposed subjects, especially in asthmatics. Positive associations were observed among mold sensitization, asthma, and mold exposure, but not in subjects with predominantly environmental sensitizations without mold sensitization. Thus, sIgE to mx1 but not sIgG to Gmx6 is a useful diagnostic marker to verify mold-associated respiratory symptoms.

Authors: Sabine Kespohl, Verena Liebers, Silke Maryska, Ursula Meurer, Claudia Litzenberger, Rolf Merget, Monika Raulf

Full Source: Allergologie select 2022 Mar 29;6:118-132. doi: 10.5414/ALX02298E.

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