

# Bulletin Board

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## Technical

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## CHEMICAL EFFECTS

## Skin remodeling and wound healing in the Gottingen Minipig following exposure to Sulfur Mustard

2020-05-20

Sulfur mustard (SM), a dermal vesicant that has been used in chemical warfare, causes inflammation, edema and epidermal erosions depending on the dose and time following exposure. Herein, a minipig model was used to characterize wound healing following dermal exposure to SM. Saturated SM vapor caps were placed on the dorsal flanks of 3-month-old male Gottingen minipigs for 30 min. After 48 h the control and SM wounded sites were debrided daily for 7 days with wet to wet saline gauze soaks. Animals were then euthanized, and full thickness skin biopsies prepared for histology and immunohistochemistry. Control skin contained a well differentiated epidermis with a prominent stratum corneum. A well-developed eschar covered the skin of SM treated animals, however, the epidermis beneath the eschar displayed significant wound healing with a hyperplastic epidermis. Stratum corneum shedding and a multilayered basal epithelium consisting of cuboidal and columnar cells were also evident in the neoepidermis. Nuclear expression of proliferating cell nuclear antigen (PCNA) was contiguous in cells along the basal epidermal layer of control and SM exposed skin; SM caused a significant increase in PCNA expression in basal and suprabasal cells. SM exposure was also associated with marked changes in expression of markers of wound healing including increases in keratin 10, keratin 17 and loricrin and decreases in E-cadherin. Trichrome staining of control skin showed a well-developed collagen network with no delineation between the papillary and reticular dermis. Conversely, a major delineation was observed in SM-exposed skin including a web-like papillary dermis composed of filamentous extracellular matrix, and compact collagen fibrils in the lower reticular dermis. Although the dermis below the wound site was disrupted, there was substantive epidermal regeneration following SM-induced injury. Further studies analyzing the wound healing process in minipig skin will be important to provide a model to evaluate potential vesicant countermeasures.

Authors: Jeffrey D Laskin, Gabriella Wahler, Claire R Crutch, Patrick J Sinko, Debra L Laskin, Diane E Heck, Laurie B Jospheh

Full Source: Experimental and molecular pathology. 2020 May 20;104470. doi: 10.1016/j.yexmp.2020.104470. Online ahead of print.

Saturated SM vapor caps were placed on the dorsal flanks of 3-month-old male Gottingen minipigs for 30 min.

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## Calreticulin regulated intrinsic apoptosis through mitochondria-dependent and independent pathways mediated by ER stress in Arsenite exposed HT-22 cells

2020-07-01

Arsenic is a naturally occurring environmental toxicant. Chronic exposure to arsenic is linked with neurological damage. Although the mechanisms remain to be elucidated, it is currently believed that neural cell apoptosis is one of the underlying mechanisms of arsenic-induced neurotoxicity. Calreticulin (CRT) is a quality control chaperone located in the lumen of the endoplasmic reticulum (ER), which participates in many signaling pathways including apoptosis. However, the role of CRT in apoptosis is controversial. Whether CRT plays a role in arsenite-induced apoptosis and the relationship between CRT and ER stress-mediated apoptosis have not been mentioned before. In this study, we found that CRT expression as well as the cell apoptosis levels increased in a dose dependent manner upon arsenite exposure in HT-22 cells, a mouse hippocampal neural cell line. In addition, arsenite exposure resulted in the up-regulation of ER stress indicator GRP78 and ER stress-related proteins including p-PERK, ATF4, CHOP, calpain2 and cleaved caspases-12, accompanied by the down-regulation of Bcl-2 and up-regulation of Bax and cleaved caspase-3. Silence of CRT remarkably alleviated arsenite-induced apoptosis and reversed the expression of the proteins above. Our findings confirmed the role of CRT in the induction of apoptosis upon arsenite exposure and suggested that CRT mediated the intrinsic apoptotic cell death including both mitochondria-dependent (PERK/ATF4/CHOP/Bcl-2) and independent (calpain2/caspases-12) pathways initiated by ER stress, which we believed to be a previously undocumented property of arsenite-induced apoptosis. Authors: Xiaotong Wang, Xudan Liu, Yao Chen, Huanhuan Wang, Ruo Zhang, Qianhui Zhang, Yuting Wei, Sainan Shi, Xin Li Full Source: Chemosphere. 2020 Jul;251:126466. doi: 10.1016/j.chemosphere.2020.126466. Epub 2020 Mar 10.

Chronic exposure to arsenic is linked with neurological damage.

## ENVIRONMENTAL RESEARCH

## Occurrences of pharmaceuticals and personal care products in the drinking water of Taiwan and their removal in conventional water treatment processes

2020-05-07

Pharmaceuticals and personal care products (PPCPs) has been of concerns for their potential threats to ecosystems and human's health for decades.

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PPCPs have been detected in water environments worldwide and have been identified in water sources and finished water. To elucidate the potential exposure of PPCPs in drinking water, this study assessed the occurrences and treatment efficiencies of PPCPs in the drinking water of Taiwan. Raw and finished water samples collected from five main drinking water treatment plants (DWTPs) in February, June, and November 2018 were analyzed. Furthermore, laboratory-scale water treatment processes were conducted to evaluate the treatment efficiencies of these chemicals. Most of the water samples from the DWTPs had a low concentration (<30 ng/L) of PPCPs. Only samples from a DWTP was observed to have higher concentration of ibuprofen (55.6 ng/L), benzophenone (92.5 ng/L), caffeine (390.5 ng/L), and diethyltoluamide (DEET) (434.9 ng/L) in raw water than others. The results of laboratory simulations indicated that the pre-chlorination process was the key step responsible for the removal of PPCPs in conventional water treatment processes, which can remove most of the hormone treatment products, parabens, oxybenzone, and acetaminophen in water sources. However, the filtration process with anthracite as a medium could remove some of the parabens (approximately 11.9%-41.2%), hormones (approximately 18.2%-44.8%), suntan lotions (37.5%-68.8%), and naproxen (30.1%) from Milli-Q water. The removal efficiencies of the aforementioned chemicals were marginally lower in raw water. However, analgesics, caffeine, and DEET cannot be removed effectively through conventional drinking water treatment. Authors: Chih-Wei Pai, Dexter Leong, Chia-Yang Chen, Gen-Shuh Wang Full Source: Chemosphere. 2020 May 7;256:127002. doi: 10.1016/j.chemosphere.2020.127002. Online ahead of print.

### Can contamination by major systemic insecticides affect the voracity of the Harlequin Ladybird?

2020-05-05

Systemic neurotoxic insecticides are widely used to control aphid pests worldwide and their potential non-target effects on aphid predators are often unknown. Behavioral responses linked to biological control services are crucial when assessing the compatibility of chemicals with biocontrol organisms. This is particularly relevant for insecticides at low and sublethal concentrations. We studied the acute toxicity and the sublethal effect on the voracity of the generalist predator *Harmonia axyridis* (Coleoptera: Coccinellidae) caused by the exposure to three systemic insecticides routinely used against aphids. The tested insecticide concentrations were the Lethal Concentration 50% ( $LC_{50}$ ), 20% ( $LC_{20}$ ) and 1% ( $LC_1$ ) estimated for the target pest *Aphis gossypii* (Hemiptera: Aphididae) in a companion

Behavioral responses linked to biological control services are crucial when assessing the compatibility of chemicals with bio-control organisms.

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study. The survival and the voracity differed among the tested chemicals and concentrations, but only thiamethoxam at  $LC_{50}$  caused a significant predator mortality, and individuals that survived showed a reduced predation rate. The predators showed a density independent functional response after the exposure to most of the insecticide-concentration combinations, while an inverse density dependence of the prey consumption rate was observed for coccinellids exposed to sulfoxaflor and thiamethoxam at their lowest tested concentration. The estimated parameters, i.e., the attack rate and the prey handling time, were affected at higher concentrations by both imidacloprid and sulfoxaflor. These findings stress the importance of carefully evaluating side effects of insecticides at very low concentrations on beneficial arthropods in the risk assessment schemes for sustainable pest control programmes.

Authors: Changchun Dai, Michele Ricupero, Roberto Puglisi, Yanhui Lu, Nicolas Desneux, Antonio Biondi, Lucia Zappalà  
Full Source:

### PHARMACEUTICAL/TOXICOLOGY

#### Dibutyl Phthalate aggravated asthma-like symptoms through oxidative stress and increasing Calcitonin gene-related peptide release

2020-05-20

Dibutyl phthalate (DBP) is one of the most ubiquitous phthalate esters found in everyday products, and is receiving increased attention as an immunologic adjuvant. However, information regarding DBP-aggravated allergic asthma is still limited. This study used a mouse model sensitized with ovalbumin (OVA) to determine any adverse effects of DBP on allergic asthma. Our results reveal that allergic asthmatic mice exposed to DBP for an extended period had a significant increase in inflammatory cell infiltration; a significant increase in levels of serum immunoglobulin and T helper 2 cell (Th2) and T helper 17 cell (Th17) cytokines in lung tissue; and significant changes in lung histology and AHR, all of which are typical asthmatic symptoms. The levels of oxidative stress and levels of the neuropeptide, calcitonin gene related peptide (CGRP), were also elevated after DBP exposure. Interestingly, blocking oxidative stress by administering melatonin (MT) not only reduced oxidative stress and CGRP levels, but also ameliorated the asthmatic symptoms. Collectively, these

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results show that DBP exacerbates asthma-like pathologies by increasing the expression of CGRP mediated by oxidative stress.

Authors: Sangyu Zhou, Man Han, Yaolin Ren, Liju Duan, Yan Zeng, Jinquan Li

Full Source: Ecotoxicology and environmental safety. 020 May 20;199:110740. doi: 10.1016/j.ecoenv.2020.110740. Online ahead of print.

### Prevention and protection measures of healthcare workers exposed in health settings to severe acute respiratory infections from SARS-COV-2 in a university hospital in Bari, Apulia Region, Southern Italy

2020-05-20

SARS-CoV-2-related SARIs (severe acute respiratory infections) have a major impact on public health; moreover, healthcare workers (HCWs) are exposed to a high biological risk. The aim of this study was to show the prevention procedures in place in the University Hospital of Bari (Apulia Region, Southern Italy) to reduce this risk to HCWs, consisting of the enhancement of preventive measures and the activation of a report system to collect HCWs' contacts. To date, 23 confirmed cases of infections (0.4% of all HCWs) have been reported in a 30-day observation period. These results show that correct management of HCWs' contacts is essential to avoid nosocomial clusters.

Authors: Vimercati Luigi, Dell'Erba Alessandro, Migliore Giovanni, De Maria Luigi, Caputi Antonio, Quarato Marco, Stefanizzi Pasquale, Cavone Domenica, Ferorelli Davide, Sponselli Stefania, Mansi Francesca, Tafuri Silvio

Full Source: The Journal of Hospital Infection. 2020 May 20;S0195-6701(20)30255-3. doi: 10.1016/j.jhin.2020.05.024. Online ahead of print.

### Chemical multi-fingerprinting of exogenous ultrafine particles in human serum and pleural effusion

2020-05-22

Ambient particulate matter pollution is one of the leading causes of global disease burden. Epidemiological studies have revealed the connections between particulate exposure and cardiovascular and respiratory diseases. However, until now, the real species of ambient ultrafine particles (UFPs) in humans are still scarcely known. Here we report the discovery and characterization of exogenous nanoparticles (NPs) in human serum and pleural effusion (PE) samples collected from non-occupational subjects in a typical polluted region. We show the wide presence of NPs in human

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serum and PE samples with extreme diversity in chemical species, concentration, and morphology. Through chemical multi-fingerprinting (including elemental fingerprints, high-resolution structural fingerprints, and stable iron isotopic fingerprints) of NPs, we identify the sources of the NPs to be abiogenic, particularly, combustion-derived particulate emission. Our results provide evidence for the translocation of ambient UFPs into the human circulatory system, and also provide information for understanding their systemic health effects.

Authors: Dawei Lu, Qian Luo, Rui Chen, Yongxun Zhuansun, Jie Jiang, Weichao Wang, Xuezhi Yang, Luyao Zhang, Xiaolei Liu, Fang Li, Qian Liu, Guibin Jiang

Full Source: Nature Communications. 2020 May 22;11(1):2567. doi: 10.1038/s41467-020-16427-x.

## OCCUPATIONAL

### Systematic review of cannabis use and risk of occupational injury

2020-05-22

Aim: A range of nations, including countries of the European Union, Australia, and the Americas have recently implemented or proposed reforms to how they control cannabis use, thereby departing from traditional approaches of criminal prohibition that have dominated throughout most of the twentieth century. Given these policy developments and the widespread global use of cannabis, it is critically important to understand the possible risks associated with cannabis use in relation to major societal harms. Methods: This systematic review investigates the potential link between cannabis use and occupational injury. Consequently, it appraises all available current literature from five databases, following Cochrane and PRISMA guidelines. Results: Seven of the 16 reviewed studies show evidence supporting a positive association between cannabis use and occupational injury. One study shows evidence supporting a negative association and the remaining eight studies show no evidence of a significant relation. None of the studies assessed cannabis-related impairment. Only three of the reviewed studies show clear evidence that cannabis use preceded the occupational-injury event. Conclusion: The current body of evidence does not provide sufficient evidence to support the position that cannabis users are at increased risk of occupational injury. Further, the study quality assessment suggests significant biases in the extant literature are present due to potential confounding variables, selection of participants, and

To date, 23 confirmed cases of infections (0.4% of all HCWs) have been reported in a 30-day observation period.

Seven of the 16 reviewed studies show evidence supporting a positive association between cannabis use and occupational injury.

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measurement of exposures and outcomes. Future high-quality evidence will be needed to elucidate the relation between cannabis use and occupational injury.

Authors: Wade R Biasutti, Kurt S H Leffers, Russell C Callaghan

Full Source: Substance use and misuse. 2020 May 22;1-13. doi:

10.1080/10826084.2020.1759643. Online ahead of print.

### Occupational noise exposure and vestibular schwannoma: A case-control study in Sweden

2020-05-22

It has been suggested that the association between self-reported occupational noise exposure and vestibular schwannoma (VS) found in several studies, represents recall bias. Therefore, we aim to study the relation in a large case-control study using occupational noise measurements. We performed a case-control study from Sweden of 1913 VS cases diagnosed in 1961-2009 and 9566 age- and sex-matched population controls. We defined occupational history by linkage to national censuses from 1960, 1970, 1980, and 1990. We estimated occupational noise exposure for each case and control using a job-exposure matrix (JEM). There was no association between occupational noise exposure and VS. Among subjects assessed as ever exposed to occupational noise levels  $\geq 85$  dB (214 cases and 1142 controls), the odds ratio for VS per five years of exposure was 1.02 (95% confidence interval 0.90-1.17). Workers with noise levels of 85 dB or higher for at least 15 years (5-year latency period), showed no increased risk of VS (odds ratio 0.98, 0.73-1.31) compared to those who had never been exposed to noise levels of 75 dB or higher. To conclude, our large study does not support an association between occupational noise exposure and VS.

Authors: Lisa Aarhus, Kristina Kj rheim, Sanna Heikkinen, Jan Iver Martinsen, Ero Pukkala, Jenny Selander, Matthias Sjöström, Øicind Sakre, Kurt Straif, Ingrid Sivesind Mehlum

Full Source: American Journal of Epidemiology. 2020 May 22;kwaa091. doi: 10.1093/aje/kwaa091. Online ahead of print.

### Long-term exposure to air pollution and incidence of myocardial infarction: a Danish nurse cohort study

2020-05-06

Background: Air pollution exposure has been linked to coronary heart disease, although evidence on PM<sub>2.5</sub> and myocardial infarction (MI) incidence is mixed.

Therefore, we aim to study the relation in a large case-control study using occupational noise measurements.

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Objectives: This prospective cohort study aimed to investigate associations between long-term exposure to air pollution and MI incidence, adjusting for road traffic noise.

Methods: We used data from the nationwide Danish Nurse Cohort on 22,882 female nurses (>44years>44years of age) who, at recruitment in 1993 or 1999, reported information on cardiovascular disease risk factors. Data on MI incidence was collected from the Danish National Patient Register until the end of 2014. Annual mean concentrations of particulate matter (PM) with a diameter  $< 2.5 \mu\text{g}/\text{m}^3$  (PM<sub>2.5</sub>), PM<sub>10</sub>, nitrogen dioxide (NO<sub>2</sub>), and nitrogen oxides (NO<sub>x</sub>) at the nurses' residences since 1990 (PM<sub>10</sub> and PM<sub>2.5</sub>) or 1970 (NO<sub>2</sub> and NO<sub>x</sub>) were estimated using the Danish Eulerian Hemispheric Model/Urban Background Model/AirGIS (DEHM/UBM/AirGIS) dispersion model. We used time-varying Cox regression models to examine the association between 1- and 3-y running means of these pollutants, as well as 23-y running means of NO<sub>2</sub> and NO<sub>x</sub>, with both overall and fatal incident MI. Associations were explored in three progressively adjusted models: Model 1, adjusted for age and baseline year; Model 2, with further adjustment for potential confounding by lifestyle and cardiovascular disease risk factors; and Model 3, with further adjustment for road traffic noise, modeled as the annual mean of a weighted 24-h average (Lden).

Results: Of the 22,882 women, 641 developed MI during a mean follow-up of 18.6 y, 121 (18.9%) of which were fatal. Reported hazard ratios (HRs) were based on interquartile range increases of 5.3, 5.5, 8.1, and 11.5  $\mu\text{g}/\text{m}^3$  for PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and NO<sub>x</sub>, respectively. In Model 1, we observed a positive association between a 3-y running mean of PM<sub>2.5</sub> and an overall incident MI with an HR=1.20 (95% CI: 1.07, 1.35), which attenuated to HR=1.06 (95% CI: 0.92, 1.23) in Model 2. In Model 1 for incident fatal MI, we observed a strong association with a 3-y running mean of PM<sub>2.5</sub>, with an HR=1.69 (95% CI: 1.33, 2.13), which attenuated to HR=1.35 (95% CI: 1.01, 1.81) in Model 2. Similar associations were seen for PM<sub>10</sub>, with 3-y, Model 2 estimates for overall and fatal incident MI of HR=1.06 (95% CI: 0.91, 1.23) and HR=1.35 (95% CI: 1.01, 1.81), respectively. No evidence of an association was observed for NO<sub>2</sub> or NO<sub>x</sub>. For all pollutants, associations in Model 2 were robust to further adjustment for road traffic noise in Model 3 and were similar for a 1-y running mean exposure.

Conclusions: We found no association between long-term exposure to PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, or NO<sub>x</sub> and overall MI incidence, but we observed positive associations

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for PM<sub>2.5</sub> and PM<sub>10</sub> with fatal MI. We present novel findings that the association between PM and MI incidence is robust to adjustment for road traffic noise. <https://doi.org/10.1289/EHP5818>.

Authors: Johannah Cramer, Jeanette T Jørgensen, Barbara Hoffman, Steffen Loft, Elvira V Bräuner, Eva Prescott, Matthias Ketzel, Ole Hertel, Jørgen Brandt, Steen S Jensen, Claus Backalarz, Mette K Simonsen, Zorana J Andersen

Full Source: Environmental health perspectives. 2020 May;128(5):57003. doi: 10.1289/EHP5818. Epub 2020 May 6.