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### PUBLIC HEALTH RESEARCH

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## Technical

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#### ENVIRONMENTAL RESEARCH

##### Transcriptomic analysis of short-term 17 $\alpha$ -ethynylestradiol exposure in two Californian sentinel fish species sardine (*Sardinops sagax*) and mackerel (*Scomber japonicus*)

2019-02-11

Endocrine disrupting chemicals (EDCs) are substances which disrupt normal functioning of the endocrine system by interfering with hormone regulated physiological pathways. Aquatic environments provide the ultimate reservoir for many EDCs as they enter rivers and the ocean via effluent discharges and accumulate in sediments. One EDC widely dispersed in municipal wastewater effluent discharges is 17 $\alpha$ -ethynylestradiol (EE2), which is one of the most widely prescribed medicines. EE2 is a bio-active estrogen employed in the majority of oral contraceptive pill formulations. As evidence of the health risks posed by EDCs mount, there is an urgent need to improve diagnostic tools for monitoring the effects of pollutants. As the cost of high throughput sequencing (HTS) diminishes, transcriptional profiling of an organism in response to EDC perturbation presents a cost-effective way of screening a wide range of endocrine responses. Coastal pelagic filter feeding fish species analysed using HTS provide an excellent tool for EDC risk assessment in the marine environment. Unfortunately, there are limited genome sequence data and annotation for many of these species including Pacific sardine (*Sardinops sagax*) and chub mackerel (*Scomber japonicus*), which limits the utility of molecular tools such as HTS to interrogate the effects of endocrine disruption. In this study, the authors performed RNA sequencing (RNAseq) of liver RNA harvested from wild sardine and mackerel exposed for 5 h under laboratory conditions to a concentration of 12.5 pM EE2 in the tank water. An analytical framework was developed for transcriptomic analyses of species with limited genomic information. EE2 exposure altered expression patterns of key genes involved in important metabolic and physiological processes. The systems approach presented here provides a powerful tool for obtaining a comprehensive picture of endocrine disruption in aquatic organisms.

Authors: Renaud L, Agarwal N, Richards DJ, Falcinelli S, Hazard ES, Carnevali O, Hyde J, Hardiman G.

Full Source: Environmental Pollution 2019 Jan; 244:926-937. doi: 10.1016/j.envpol.2018.10.058. Epub 2018 Oct 20.

In this study, the authors performed RNA sequencing (RNAseq) of liver RNA harvested from wild sardine and mackerel exposed for 5 h under laboratory conditions to a concentration of 12.5 pM EE2 in the tank water.

### Direct quantitation and characterization of fatty acids in salmon tissue by condensed phase membrane introduction mass spectrometry (CP-MIMS) using a modified donor phase

2019-02-11

Existing mass spectrometric methods for the analysis of fatty acids often require derivatisation, chromatographic separations, and/or extensive sample preparation. Direct mass spectrometry strategies can avoid these requirements, but may also suffer from poor quantitation and/or lack of sensitivity. Condensed phase-membrane introduction mass spectrometry (CP-MIMS) provides direct quantitative measurements of analytes in complex samples with little or no sample preparation. CP-MIMS uses a semipermeable membrane to transfer neutral hydrophobic compounds from real-world samples to a mass spectrometer. The results presented utilise aqueous/organic sample solvent (donor) mixtures to allow for the sensitive (ppt) detection of a range of fatty acids. The relative sensitivity across a homologous series of fatty acids is observed to change, favouring short- or long-chain fatty acids, depending on the amount of miscible co-solvent added to the donor phase. Further, lithium acetate added online via the acceptor phase was used in tandem mass spectrometry experiments to determine the location of double bonds in polyunsaturated fatty acids (PUFAs). The method was applied to direct measurements and structural determinations for selected PUFAs in salmon tissue samples. Standard addition was employed to quantify the amount of PUFAs in a variety of salmon samples, yielding 0.27-0.42 and 0.40-0.84 w/w % for eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), respectively, for Sockeye and Chinook salmon, in good agreement with the literature. This study presents, to our knowledge, the first use of CP-MIMS for the direct analysis of fatty acids in oily foodstuff samples.

Authors: Borden SA, Damer HN, Krogh ET, Gill CG.

Full Source: Analytical and Bioanalytical Chemistry. 2018 Nov 23. doi: 10.1007/s00216-018-1467-y. [Epub ahead of print]

In agriculture and urban wells, the authors identified DDT and organochlorine pesticides, as well as myclobutanil

### Emerging contaminants and nutrients in a saline aquifer of a complex environment

2019-02-11

The quality and availability of water has become a pressing issue worldwide, being particularly important in semi-arid regions, where climate change has aggravated the problem. The use of anthropogenic chemicals, classified as emerging pollutants, adds to the problem

representing a treat, since they are not regulated and have a potential impact on human and environmental health. This pressing problem has not been studied widely in complex environments like the one presented in this study. Distribution and seasonal variability of faecal sterols, alkylphenols, pesticides (emerging pollutants) and nutrients were determined in 35 wells used for agriculture and human consumption in the Valley of Maneadero, located in the semi-arid region of Baja California, Mexico. The presence of the tested pollutants in the saline aquifer was heterogeneous, showing important differences in concentration and distribution. Wells destined for household use showed the highest variability. In these wells, anthropogenic faecal sterols were detected and, alkylphenols, such as octylphenol and nonylphenol had maximum concentrations (2.7 ng/mL). In agriculture and urban wells, the authors identified DDT and organochlorine pesticides, as well as myclobutanil, which is considered a modern pesticide. Nitrates were identified in concentrations above international standards, mainly during the dry season, in both the agricultural and urban areas. As emerging pollutants represent a negative effect on environmental and human health, this is the first paper showing the importance of measuring this type of pollutant in agricultural/semi-urban areas, especially in aquifers that have been overexploited and communities that have relied on the use of septic tanks for decades.

Authors: González-Acevedo ZI, García-Zarate MA, Flores-Lugo IP.

Full Source: Environmental Pollution. 2019 Jan; 244:885-897. doi: 10.1016/j.envpol.2018.10.104. Epub 2018 Oct 27.

### Plastic Pirates sample litter at rivers in Germany - Riverside litter and litter sources estimated by schoolchildren

2019-02-11

Rivers are an important source of marine anthropogenic litter, but the particular origins of riverine litter itself have not been well established. In the present study, the authors used a citizen science approach where schoolchildren examined litter at riversides and identified possible sources at over 250 sampling spots along large and small rivers in Germany, during autumn 2016 and spring 2017. Litter densities have an overall median of 0.14, interquartile range 0-0.57 items m<sup>-2</sup> and an overall average ( $\pm$ standard deviation) of  $0.54 \pm 1.20$  litter items m<sup>-2</sup>. Litter quantities differed only little by sampling year. The principal litter types found were plastics and cigarette butts (31% and 20%, respectively), followed by glass, paper, and metal items, indicating recreational visitors as the principal litter source. At many sites (85%), accumulations of litter, consisting

In the present study, the authors used a citizen science approach where schoolchildren examined litter at riversides and identified possible sources at over 250 sampling spots along large and small rivers in Germany

principally of cigarettes and food packaging, have been found. At almost all sampling sites (89%), litter potentially hazardous to human health has been observed, including broken glass, sharp metal objects, used personal hygiene articles and items containing chemicals. In the search for litter sources, the schoolchildren identified mainly people who use the rivers as recreational areas (in contrast to residents living in the vicinity, illegal dumping, or the river itself depositing litter from upstream sources). These results indicate the urgent need for better education and policy measures in order to protect riparian environments and reduce input of riverine litter to the marine environment.

Authors: Kiessling T, Knickmeier K, Kruse K, Brennecke D, Nauendorf A, Thiel M.

Full Source: Environmental Pollution. 2018 Nov 13; 245:545-557. doi: 10.1016/j.envpol.2018.11.025. [Epub ahead of print]

### Impact of an immunosuppressive human pharmaceutical on the interaction of a bacterial parasite and its invertebrate host

2019-02-11

The interaction of pollutants and pathogens may result in altered and often enhanced effects of the chemical, the biotic stressor or both. These interaction effects cannot be reliably predicted from the toxicity of the chemical or the virulence of the pathogen alone. While standardised detection methods for immunotoxic effects of chemicals exist with regard to human health, employing host-resistance assays with vertebrates, such standardised test systems are completely lacking for invertebrate species and no guidance is available on how immunotoxic effects of a chemical in invertebrates could be definitively identified. In the present study, the authors investigated the impact of the immunosuppressive pharmaceutical cyclosporine A (CsA) on the invertebrate host-pathogen system *Daphnia magna* - *Pasteuria ramosa*. CsA is a calcineurin-inhibitor in vertebrates and also known to have antibiotic as well as antifungal properties. Juvenile *D. magna* were exposed to CsA for 21 days with or without additional pathogen challenge during the first 72 h of exposure. Long-term survival of the host *D. magna* was synergistically impacted by co-exposure to the chemical and the pathogen, expressed e.g. in significantly enhanced hazard ratios. Additionally, enhanced virulence of the pathogen upon chemical co-exposure was expressed in an increased proportion of infected hosts and an increased speed of *Pasteuria*-induced host sterilisation. In contrast, effects on reproduction were additive in *Pasteuria*-challenged, but finally non-infected *D. magna*. The enhancing

In the present study, the authors investigated the impact of the immunosuppressive pharmaceutical cyclosporine A (CsA) on the invertebrate host-pathogen system *Daphnia magna* - *Pasteuria ramosa*

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effects of CsA occurred at and below 3  $\mu\text{g/L}$ , which was in the absence of the pathogen the lowest concentration significantly impacting the standard toxicity endpoint 'reproduction' in *D. magna*. The authors concluded that the present study provides evidence that a pharmaceutical intended to suppress the human immune system can also suppress disease resistance of an aquatic invertebrate organism at otherwise non-toxic concentrations. Plausible ways of direct interactions of CsA with the host's immune system are discussed, e.g. interference with phagocytosis or Toll-like receptors. Experimental verification of such a direct interference would be warranted to support the strong evidence for immunotoxic activity of CsA in invertebrates. While it remains open whether CsA concentrations in the environment are high enough to trigger adverse effects in environmental organisms, the findings highlight the need to consider immunotoxicity in an environmental risk assessment, and to develop suitable standardised methods for this purpose.

Authors: Schlüter-Vorberg L, Coors A.

Full Source: *Aquatic Toxicology*. 2018 Nov 14; 206:91-101. doi: 10.1016/j.aquatox.2018.11.007. [Epub ahead of print]

## MEDICAL RESEARCH

**A new analytical framework for multi-residue analysis of chemically diverse endocrine disruptors in complex environmental matrices utilising ultra-performance liquid chromatography coupled with high-resolution tandem quadrupole time-of-flight mass spectrometry**

2019-02-11

This study presents a comprehensive analytical framework for identification and quantification of chemically diverse endocrine disrupting chemicals (EDCs) used in personal care and consumer products in diverse solid and liquid environmental matrices with an ultimate goal of evaluating public exposure to EDCs via water fingerprinting. Liquid chromatography coupled with tandem quadrupole time-of-flight mass spectrometry (UHPLC-ESI-MS/MS) was used for targeted analysis of selected EDCs as well as to identify and quantify a few metabolites using post-acquisition data mining. Solid-phase extraction (SPE) was applied to liquid matrices in order to reduce matrix effects and provide required sample concentration and ultimately, high sensitivity and selectivity of measurements. SPE recoveries in liquid samples ranged from 49 to 140% with method quantification limits not exceeding 1 ng L<sup>-1</sup> for the

**This study presents a comprehensive analytical framework for identification and quantification of chemically diverse endocrine disrupting chemicals (EDCs) used in personal care and consumer products**

majority of EDCs. Microwave-assisted extraction (MAE) was applied to solid samples and when followed by SPE, it permitted the analysis of EDCs in digested sludge. MAE/SPE recoveries varied from 11 to 186% and MQLs between 0.03 and 8.1 ng g<sup>-1</sup> with the majority of compounds showing MQLs below 2 ng g<sup>-1</sup>. Mass error for quantifier and qualifier ions was below 5 ppm when analysing river water and effluent wastewater and below 10 ppm when analysing influent wastewater and solid samples. The method was successfully applied to environmental samples, with 33 EDCs identified and quantified in wastewater and receiving waters. In addition, several EDCs were found in digested sludge, which confirms that for a more comprehensive understanding of exposure patterns and environmental impact, analysis of solids cannot be neglected. Finally, post-acquisition data mining permitted the identification and quantification of a metabolite of BPA and the identification of a metabolite of 4-Cl-3-methylphenol. Graphical abstract.

Authors: Lopardo L, Rydevik A, Kasprzyk-Hordern B.

Full Source: Analytical and Bioanalytical Chemistry. 2018 Nov 22. doi: 10.1007/s00216-018-1483-y. [Epub ahead of print]

### Andexanet alfa in the treatment of acute major bleeding related to apixaban and rivaroxaban: a profile of its use in the USA

2019-02-11

Andexanet alfa (Andexxa®), a first-in-class recombinant modified factor Xa protein, is currently the only specific agent available to reverse life-threatening or uncontrolled bleeding with the factor Xa inhibitors apixaban and rivaroxaban. Andexanet alfa acts as a decoy and competes with endogenous factor Xa to bind factor Xa inhibitors, thereby reversing the anticoagulant effects of factor Xa inhibitors, and restoring the activity of endogenous factor Xa. In adults with major bleeding associated with the use of apixaban or rivaroxaban, intravenous administration of andexanet alfa effectively and rapidly reduces anti-factor Xa levels, with reduced levels being maintained during continued treatment. The tolerability profile of andexanet alfa in patients is generally similar to that reported of other approved anticoagulation reversal agents. With the known increased risk of thromboembolic events following andexanet alfa treatment, anticoagulant therapy should be resumed as soon as medically appropriate.

Author: Heo YA.

Full Source: Drugs & Therapy Perspectives. 2018;34(11):507-512. doi: 10.1007/s40267-018-0561-8. Epub 2018 Oct 5.

### Burosumab in X-linked hypophosphatemia: a profile of its use in the USA

2019-02-11

Burosumab (Crysvita®), a fully human IgG1 monoclonal antibody directed at fibroblast growth factor 23 (FGF23), is indicated for the treatment of X-linked hypophosphatemia (XLH), a condition associated with excessive FGF23 production. It directly addresses the excessive FGF23 activity in patients with XLH by binding to FGF23, and inhibiting its signalling. This leads to increased gastrointestinal phosphate absorption and renal phosphate reabsorption, thereby improving serum phosphate levels, and, ultimately, bone mineralisation and the risk of bone disease. In clinical trials, subcutaneous burosumab increased serum phosphorus levels in paediatric and adult patients with XLH, as well as significantly improving the severity of rickets in children, and improving pain, stiffness, physical functioning, and fracture/pseudofracture healing in adults. Burosumab is well tolerated by children and adults with XLH, with most treatment-emergent adverse events being of mild to moderate severity.

Author: Lyseng-Williamson KA.

Full Source: *Drugs & Therapy Perspectives* 2018;34(11):497-506. doi: 10.1007/s40267-018-0560-9. Epub 2018 Oct 8.

### Effect of erlotinib plus bevacizumab on brain metastases in patients with non-small cell lung cancer

2019-02-11

The standard therapy for brain metastasis (BM) in non-small cell lung cancer (NSCLC) is radiation therapy (RT), although it is associated with complications such as leukoencephalopathy. In the current study, the authors retrospectively review data from eight patients who had NSCLC and harboured epidermal growth factor receptor (EGFR) mutations, and who were received erlotinib plus bevacizumab (E+B) as first-line therapy for BM. Patients were given E+B as first therapy for BM until August 2017 at our institution. Patients receiving local therapy for BM, such as surgery or radiotherapy, were excluded. Patients were administered erlotinib orally (once daily at 150 mg/body) plus bevacizumab by intravenous infusion (15 mg/kg on day 1 of a 21- or 28-day cycle). Eight NSCLC patients who were diagnosed with BM received E+B, including 2 men and 6 women with a median age of 65 years (range, 46-84 years). Four patients had an L858R EGFR mutation, while the other four had an exon 19 deletion. Seven patients had a partial response to E+B treatment, and one had a complete response. The 2-year survival rate was 62.5%. Three patients who were

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pre-treated with gefitinib had an E+B treatment duration of less than 1 year. At the time of this analysis, four patients had BM-related neurologic symptoms and multiple BMs, and were still receiving E+B with no evidence of treatment failure after more than 1 year. E+B can be used as first-line therapy for BM, even in patients with BM-related neurologic symptoms and multiple BMs.

Authors: Chikaishi Y, Kanayama M, Taira A, Nabe Y, Shinohara S, Kuwata T, Takenaka M, Oka S, Hirai A, Kuroda K, Imanishi N, Ichiki Y, Tanaka F.

Full Source: *The Annals of Translational Medicine*. 2018 Oct; 6(20):401. doi: 10.21037/atm.2018.09.33.

### Antibody-initiated beneficial and harmful immune responses

2019-02-11

A critical function of the immune system is to maintain tolerance to self by corrective immune responses throughout life, including preventing or correcting changes that may interfere with organ function and architectural integrity. These changes have two broad categories, namely (1) exogenous antigen-induced mishaps (e.g., due to bacterial, viral or fungal infections) and (2) endogenous antigen-caused ailments initiated by modified self-antigens derived from damaged organs following exposure to smoke, certain drugs, chemicals, infectious agents, radiation, etc., resulting in autoimmune diseases or cancer. In some cases, cells of the immune system are unable to respond with a corrective antibody response. For example, presentation of a modified self-antigen can initiate a pathogenic IgG immune response, thereby causing an autoimmune disease. Furthermore, if cancer-associated antigens are not appropriately presented to the cells of the immune system, there is failure to mount a specific pathogenic lytic IgG autoantibody response for recognition and elimination of cancer-associated antigens, and as a consequence, the cancer continues to proliferate. The third vaccination technique that we have developed and designated a modified vaccination technique (MVT) is able to correct these immunological mishaps. The premise of the MVT is that it can prevent both exogenous (infectious and contagious diseases) and endogenous (autoimmune diseases and cancer) antigen-caused diseases, as well as terminate established diseases. Therefore, by exploiting the immune system's natural abilities to make corrective responses, it has both prophylactic and therapeutic actions, with minimal side effects.

Authors: Barabas AZ, Cole CD, Lafreniere R.

Full Source: *Immunologic Research*. 2018 Nov 19. doi: 10.1007/s12026-018-9037-0. [Epub ahead of print]

A critical function of the immune system is to maintain tolerance to self by corrective immune responses throughout life, including preventing or correcting changes that may interfere with organ function and architectural integrity.

### OCCUPATIONAL RESEARCH

#### Silicosis in underground miners in Lubumbashi, Democratic Republic of the Congo: 27 cases

2019-02-12

Silicosis is one of the most prevalent occupational lung diseases and a public health problem throughout the world. Underground miners of copper and cobalt are exposed to the dust of these minerals and thus to the risk of developing silicosis. The objective of this study was to describe a series of silicosis cases in miners exposed to mineral dusts at a mining company operating since the colonial era in Lubumbashi, Katanga province, in the Democratic Republic of the Congo (DRC). This descriptive retrospective study reviewed records at the occupational safety and health department of the mining company mentioned above and included 2500 underground miners who worked there between 1970 and 1995; it collected and analysed their medical records. Chest radiographs of silicosis patients were classified according to the ILO International Classification of Radiographs of Pneumoconiosis. All miners were males (mean age:  $48.5 \pm 12.5$ ), had low literacy levels, and used no protective device (i.e., mask) against dust. Their mean number of working years in the underground mines was  $25.07 \pm 7.39$  years. Of the 2500 miners, 1.08 % (27/2,500) had developed silicosis. The most common clinical manifestations were dyspnoea and cough, and the most prevalent radiologic features large opacities (92.59%), small opacities (96.27%), and pleural thickening (25.92%). The fatality rate was 100%. This study revealed the absence of safety measures among Congolese underground miners from Lubumbashi, which might have contributed to the development of silicosis in some of them. It is thus necessary to implement occupational safety measures to reduce their risk of silicosis.

Authors: Kabamba Ngombe L, Nlandu Ngatu R, Nyembo Mukena C, Kabyla Ilunga B, Wembonyama Okitotsho S, Kakoma Sakatolo JB, Luboya Numbi O, Danuser B.

Full Source: Médecine et santé tropicales. 2018 Nov 29. doi: 10.1684/mst.2018.0812. [Epub ahead of print]

#### Contact dermatitis and sensitisation in professional musicians

2019-02-12

Professional musicians have prolonged and intense physical contact with their instruments. This can lead to occupational skin diseases,

The objective of this study was to describe a series of silicosis cases in miners exposed to mineral dusts at a mining company operating since the colonial era in Lubumbashi, Katanga province, in the Democratic Republic of the Congo

particularly irritant and allergic contact dermatitis. This study assessed the skin diseases and sensitisation patterns common among professional musicians. A retrospective analysis of the data of the Information Network of Departments of Dermatology (IVDK) was performed, including data from 1997 to 2017.

236 professional musicians were identified. In this group, male sex (58.6%) and younger age (60.6% aged < 40 years) were common. The musicians suffered more frequently from facial dermatitis (23.7% vs 15.7%) and less often from leg dermatitis (5.1% vs 10.7%) than the control group (the non-musicians in the IVDK database). The most frequent diagnoses were allergic contact dermatitis, atopic dermatitis, and irritant contact dermatitis. The sensitisation profile of the professional musicians was similar to that of the control group. In 8.9% of cases, an occupational background of skin disease was confirmed. Severe occupational skin diseases among professional musicians are not as common as in classic "skin-damaging" professions. However, as these skin conditions can mostly be controlled with simple preventive measures, it is recommended that this group should be patch tested and treated by a specialist.

Authors: Kraft M, Schubert S, Geier J, Worm M; IVDK.

Collaborators: Beiteke U, Dissemond J, Buhl T, Schäkel K, Pfohler C, Brasch J, Worm M, Bauer A, Kreft B, Schliemann S, Darsow U, Becker D, Forchhammer S, Hartmann K, Witte J, Pfützner W, Coras-Stepanek B, Skudlik C, Wagner N, Aberer W, Emmert S, Baron JM, Siedlecki K, Baur V, Schmieder A, Weisshaar E, Grunwald-Delitz H, Trautmann A, Bircher A, Szliska C, Weiß J, Effendy I, Jünger M, Brehler R, Molin S, Werfel T, Dickel H, Rieker-Schwienbacher J, Vieluf D, Stadler R, Simon D, Fartasch M, Navarini A, Treudler R, Nestoris S, Mechtel D, Schröder-Kraft C, Löffler H, Fischer M, Koch A, Raap U, Grabbe J, di Lucca J, Zutt M, Spring P, Prager W.

Full Source: Contact Dermatitis. 2018 Nov 29. doi: 10.1111/cod.13191.

[Epub ahead of print]

This study employs a computational experiment approach to construct an experimental platform based on multiagent interactions.

### Study on the Influence of Government Intervention on the Occupational Health and Safety (OHS) Services of Small- and Medium-Sized Enterprises (SMEs).

2019-02-12

The OHS services of SMEs are still in their start-up stage in China. As such, there is an absence of mature market norms, which in turn makes it difficult to guarantee the quality of OHS services. The government, as the "night watchman" of the market, is supposed to not only involve itself in the regulation of OHS service quality, but also introduce and implement proper regulatory strategies. This study employs a computational

experiment approach to construct an experimental platform based on multiagent interactions. By simulating the OHS service transaction activities of SMEs, this paper takes the perspective of dynamic evolution. From this perspective, the authors probe into the optimal regulatory strategy covering the positive influence of government punishment, policy supports, and service quality ratings of the OHS services of SMEs. These strategies should be built on the foundation of proper punishment standard and intensity, proper support standard and intensity, and quality rating information disclosure.

Authors: Zhang J, Mei Q, Liu S, Wang Q.

Full Source: Biomed Research International. 2018 Oct 25; 2018:5014859.

doi: 10.1155/2018/5014859. eCollection 2018.

### Work-Related Stressors and Increased Risk of Benzodiazepine Long-Term Use: Findings From the CONSTANCES Population-Based Cohort

2019-02-12

This study examined whether stressful job exposure to the public could be associated with having long-term benzodiazepine use. From the participants included between 2012 and 2016 in the French population-based CONSTANCES cohort, 13 934 men and 19 261 women declared a daily job exposure to the public and rated the frequency of stressful exposure. The authors examined benzodiazepine long-term use by using drug reimbursement administrative registries. Logistic regressions provided odds ratios (ORs) of benzodiazepine long-term use, with stratification for gender and adjustment for age, education, and area deprivation index. Occupational grade, job strain, depression, self-rated health, and alcohol use disorder were additional stratification variables. Benzodiazepine long-term use was positively associated with stressful exposure to the public ("often or always" vs "rarely or never") in men (OR= 2.2; 95% confidence interval [CI]= 1.8, 2.8) and women (OR= 1.6; 95% CI= 1.4, 1.9), with dose-dependent relationships (P trends < .001). Adjustments and analyses in subgroups without other individual or environmental vulnerability factors led to similar results. The authors concluded that stressful job exposure to the public increases the risk of benzodiazepine long-term use. Prevention programs aiming at reducing

This study examined whether stressful job exposure to the public could be associated with having long-term benzodiazepine use.

the burden of benzodiazepine long-term use would benefit in targeting this specific population.

Authors: Airagnes G, Lemogne C, Olekhnovitch R, Roquelaure Y, Hoertel N, Goldberg M, Limosin F, Zins M.

Full Source: American Journal of Public Health. 2018 Nov 29; e1-e7. doi: 10.2105/AJPH.2018.304734. [Epub ahead of print]

### Analytical strategies for assessing occupational exposure to antineoplastic drugs in healthcare workplaces

2019-02-12

Cytotoxic antineoplastic drugs (ADs), widely used in treating cancer, are considered hazardous in the workplace and thus require safe handling practices. An analytical protocol for environmental and biological AD monitoring in the healthcare environment has been developed, since Europe lacks clear guidelines and regulations for cytostatic preparation and handling. Liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used for measuring contemporaneously 20 multi-class cytostatic compounds and urinary  $\alpha$ -fluoro- $\beta$ -alanine, whereas platinum was detected by inductively coupled plasma mass spectrometry (ICP-MS). Sampling procedures and analytical conditions were optimised and the assays were validated. Environmental AD monitoring data, collected in 2009-2017, for a total of 3749 wipe tests and 57 720 determinations, was evaluated. The proportion of positive samples gradually decreased from 11.7% in 2010 to 1% in 2017, however, 2266 determinations were positive. No urine sample had detectable concentrations of any of the 4 drugs considered (0/398 samples). The authors concluded that these improvements are so large that the key role played by the new, more stringent rules for preparing and administering ADs is evident. Hence, the analytical method involving multi-element determinations allows for a more thorough and complete investigation into the AD contamination of work environments.

Authors: Dugheri S, Bonari A, Pompilio I, Boccalon P, Tognoni D, Cecchi M, Ughi M, Mucci N, Arcangeli G.

Full Source: Medycyna pracy. 2018 Dec 18;69(6):589-604. doi: 10.13075/mp.5893.00724. Epub 2018 Nov 29.

Cytotoxic antineoplastic drugs (ADs), widely used in treating cancer, are considered hazardous in the workplace and thus require safe handling practices.

### PUBLIC HEALTH RESEARCH

Advice on assistance and protection from the Scientific Advisory Board of the Organisation for the Prohibition of Chemical Weapons: Part 2. On preventing and treating health effects from acute, prolonged, and repeated nerve agent exposure, and the identification of medical countermeasures able to reduce or eliminate the longer-term health effects of nerve agents

2019-02-12

The Scientific Advisory Board (SAB) of the Organisation for the Prohibition of Chemical Weapons (OPCW) has provided advice in relation to the Chemical Weapons Convention on assistance and protection. In this study, the authors present the SAB's response to a request from the OPCW Director-General in 2014 for information on the best practices for preventing and treating the health effects from acute, prolonged, and repeated organophosphorus nerve agent (NA) exposure. The report summarises pre- and post-exposure treatments, and developments in decontaminants and adsorbing materials, that at the time of the advice, were available for NAs. The updated information provided could assist medics and emergency responders unfamiliar with treatment and decontamination options related to exposure to NAs. The SAB recommended that developments in research on medical countermeasures and decontaminants for NAs should be monitored by the OPCW, and used in assistance and protection training courses and workshops organised through its capacity building programs.

Authors: Timperley CM, Abdollahi M, Al-Amri AS, Baulig A, Benachour D, Borrett V, Cariño FA, Geist M, Gonzalez D, Kane W, Kovarik Z, Martínez-Álvarez R, Fusaro Mourão NM, Neffe S, Raza SK, Rubaylo V, Suárez AG, Takeuchi K, Tang C, Trifirò F, van Straten FM, Vanninen PS, Vučinić S, Zaitsev V, Zafar-Uz-Zaman M, Zina MS, Holen S, Forman JE, Alwan WS, Suri V.  
Full Source: Toxicology. 2019 Feb 1; 413:13-23. doi: 10.1016/j.tox.2018.11.009. Epub 2018 Nov 27.

In this study, the authors present the Scientific Advisory Board's response to a request from the OPCW Director-General in 2014 for information on the best practices for preventing and treating the health effects from acute, prolonged, and repeated organophosphorus nerve agent (NA) exposure.

The History of the Dioxin issue in Brazil: From citrus pulp crisis to food monitoring

2019-02-12

Dioxins and furans are ubiquitous, anthropogenic environmental contaminants which can be found even in isolated places. Exposition to

these chemicals poses several risks to humans such as thyroid dysfunction, cardiovascular diseases, and even cancer. In this review, the dioxin issue is analysed in the light of the events that brought the World's attention to these pollutants, and the evolution of Brazilian scientific data on this matter since the citrus pulp crisis in 1998. Soil and air have been the main environmental matrices studied in Brazil. However, most of the research focuses on contaminated areas, with few or no data available on background levels. With the ratification of the Stockholm Convention in 2010, Brazil started to implement some measures to monitor the release of dioxins to the environment, such as the national inventory of sources. Still, the country lacks specific legislation stating acceptable limits for some industrial processes known to be source of dioxins emissions. Likewise, food monitoring has grown in recent years with the expansion of food groups monitored in the National Control Plan for Residues and Contaminants, but the available data do not allow affirming whether Brazilian residents are safe, as regard to exposure via food consumption. The implementation of a systemic survey such as a Total Diet Study would be a good strategy for a long-term monitoring not only for dioxins but also for other contaminants. Unfortunately, progressive cuts in science funds are holding back the scientific production in Brazil, whereas worldwide new emerging contaminants are being monitored and included in National Monitoring Plans both on food and environment matrices.

Author: Lacerda JPA.

Full Source: Environment International. 2018 Nov 15. pii: S0160-4120(18)32010-5. doi: 10.1016/j.envint.2018.11.016. [Epub ahead of print]

### Child's buccal cell mitochondrial DNA content modifies the association between heart rate variability and recent air pollution exposure at school

2019-02-12

Studies investigating short-term exposure to ambient air pollution and heart rate variability (HRV) suggest that particulate matter (PM) exposure is associated with reductions in measures of HRV. Mitochondria are sensitive to PM exposure and may represent a biologically relevant underlying mechanism. However, evidence in children is lacking. In the present study, the authors examine whether PM has an influence on children's HRV and evaluate whether mitochondrial DNA content (mtDNAC) reflects individual susceptibility. Within a panel study in primary school children (aged 9-12 years), HRV was measured in a subset of 60 children on three different days during school-time using four indicators: normal-to-normal intervals (SDNN), square root of mean squared

In the present study, the authors examine whether particulate matter has an influence on children's heart rate variability and evaluate whether mitochondrial DNA content (mtDNAC) reflects individual susceptibility.

difference of normal-to-normal intervals (rMSSD), high frequency (HF), and low frequency (LF). This resulted in a total number of 150 visits (median number of visits per child: 2.5/child). MtDNAc was measured using qPCR in buccal cells. Recent PM exposure was measured at the school. Residential 24-hour mean exposure to PM was modelled with a high resolution spatial temporal model. Mixed-effects models were used to estimate the association between HRV and recent PM exposure and potential effect-modification by mtDNAc. Children were on average [SD] 9.9 [1.2] years and comprised 39 girls. Median [25th-75th] recent outdoor PM<sub>2.5</sub> and PM<sub>10</sub> exposure at school was 6.20 [2.8-12.8]  $\mu\text{g}/\text{m}^3$  and 29.3 [24.7-42.0]  $\mu\text{g}/\text{m}^3$ , respectively. In children with low mtDNAc (25th percentile), the authors observed for each 10  $\mu\text{g}/\text{m}^3$  increment in recent PM<sub>2.5</sub> exposure a lowering in the LF parameter with 9.76% (95% CI: -16.9 to -1.99%,  $p = 0.02$ ; pint = 0.007). Children with high mtDNAc did not show this association. For PM<sub>10</sub> exposure, we observed an inverse association with three HRV indicators in children with low mtDNAc: -2.24% (95% CI: -4.27 to -0.16%;  $p = 0.04$ ; pint = 0.02) for SDNN, -5.67% (95% CI: -10.5 to -0.59%;  $p = 0.03$ ; pint = 0.04) for HF and -6.64% (95% CI: -10.7 to -2.38%;  $p = 0.003$ ; pint = 0.005) for LF. The authors concluded that HRV is inversely associated with recent PM air pollution, especially in children with low mtDNAc. Our data revealed that mtDNAc determines susceptibility to adverse autonomic effects of recent PM exposure in children.

Authors: Saenen ND, Provost EB, Cuyper A, Kicinski M, Pieters N, Plusquin M, Vrijens K, De Boever P, Nawrot TS.

Full Source: Environment International. 2019 Feb; 123:39-49. doi: 10.1016/j.envint.2018.11.028. Epub 2018 Nov 26.

### Diesel exhaust, respirable dust, and ischemic heart disease: an application of the parametric g-formula

2019-02-12

Although general population studies of air pollution suggest that particulate matter - diesel exhaust emissions in particular - is a potential risk factor for cardiovascular disease, direct evidence from occupational cohorts using quantitative metrics of exposure is limited. In this study, the authors assessed counterfactual risk of ischemic heart disease (IHD) mortality under hypothetical scenarios limiting exposure levels of diesel exhaust and of respirable mine/ore dust in the Diesel Exhaust in Miners Study (DEMS) cohort.

Data on 10,779 male miners from 8 non-metal, non-coal mines - hired after diesel equipment was introduced in the respective facilities were analysed- and followed from 1948 to 1997, with 297 observed IHD deaths

In this study, the authors assessed counterfactual risk of ischemic heart disease (IHD) mortality under hypothetical scenarios limiting exposure levels of diesel exhaust and of respirable mine/ore dust in the Diesel Exhaust in Miners Study (DEMS) cohort.

in this sample. The parametric g-formula was applied to assess risk under hypothetical scenarios with various limits for respirable elemental carbon (a surrogate for diesel exhaust), and respirable dust, separately and jointly. The risk ratio comparing the observed risk to cumulative IHD mortality risk at age 80 under a hypothetical scenario where exposures to elemental carbon and respirable dust are eliminated was 0.79 (95% confidence interval (CI): 0.64, 0.97). The corresponding risk difference was -3.0% (95% CI: -5.7, -0.3). The authors concluded that the findings, based on data from a cohort of non-metal miners, are consistent with the hypothesis that interventions to eliminate exposures to diesel exhaust and respirable dust would reduce IHD mortality risk.

Authors: Neophytou AM, Costello S, Picciotto S, Brown DM, Attfield MD, Blair A, Lubin JH, Stewart PA, Vermeulen R, Silverman DT, Eisen EA.

Full Source: *Epidemiology*. 2018 Nov 27. doi: 10.1097/EDE.0000000000000954. [Epub ahead of print]

### Opening windows and closing gaps: a case analysis of Canada's 2009 tobacco additives ban and its policy lessons

2019-02-12

In 2009, Canada adopted legislation (Bill C-32) restricting the sale of flavoured tobacco products, one of the first in the world. This study examines the agenda-setting process leading to the adoption of Bill C-32. This research was conducted using a case study design informed by Kingdon's Multiple Streams framework and Hecló's policy learning approach. In-depth interviews were conducted with key informants from government, health-based non-governmental organizations (NGOs), trade associations and the cigar manufacturing sector (n = 11). Public documents produced by media (n = 19), government (n = 11), NGOs (n = 15), as well as technical reports (n = 8) and formal stakeholder submissions (n = 137) were included for analysis. Data were coded with the objective of understanding key events or moments in the lead up to the adoption of Bill C-32 and the actors and arguments in support of and opposition to Bill C-32. The findings point to the importance of a small but active group of NGOs who worked to publicise the issue and eventually take advantage of an open policy window. This analysis also illustrates that even though consensus was developed about the policy problem and civil society was able to garner political support to address the problem, disagreement and dissent pertaining to the technical dimensions of the policy solution created loopholes for the tobacco industry to exploit. NGOs remain a critical factor in efforts to strengthen tobacco control policy. These organisations were able to mobilise support for the tobacco flavouring

In 2009, Canada adopted legislation (Bill C-32) restricting the sale of flavoured tobacco products, one of the first in the world.

## Technical

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ban adopted at the Federal level in Canada, and although the initial Bill had major limitations to achieving the health objectives, the persistence of these NGOs resulted in amendments to close these loopholes.

Authors: Lencucha R, Ruckert A, Labonte R, Drope J.

Full Source: BMC Public Health. 2018 Nov 28;18(1):1321. doi: 10.1186/s12889-018-6157-3.