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Technical

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ENVIRONMENTAL RESEARCH

Apex marine predators and ocean health: Proactive screening of halogenated organic contaminants reveals ecosystem indicator species

2019-04-01

Despite decades-long bans on the production and use of certain chemicals, many halogenated organic compounds (HOCs) are persistent and can bioaccumulate in the marine environment with the potential to cause physiological harm to marine fauna. Highly lipid-rich tissue (e.g., marine mammal blubber) functions as a reservoir for HOCs, and selecting ideal indicator species is a priority for retrospective and proactive screening efforts. In the present study, the authors selected five marine mammal species as possible indicators for the Southern California Bight (SCB) and applied a non-targeted analytical method paired with an automated data reduction strategy to catalogue a broad range of known, known but unexpected, and unknown compounds in their blubber. A total of 194 HOCs were detected across the study species ($n = 25$ individuals), 81% of which are not routinely monitored, including 30 halogenated natural products and 45 compounds of unknown structure and origin. The cetacean species (long-beaked common dolphin, short-beaked common dolphin, and Risso's dolphin) averaged 128 HOCs, whereas pinnipeds (California sea lion and Pacific harbor seal) averaged 47 HOCs. The authors suspect this disparity can be attributed to differences in life history, foraging strategies, and/or enzyme-mediated metabolism. The results support proposing (1) the long- and short-beaked common dolphin as apex marine predator sentinels for future and retrospective biomonitoring of the SCB ecosystem and (2) the use of non-targeted contaminant analyses to identify and prioritize emerging contaminants. The use of a sentinel marine species together with the non-targeted analytical approach will enable a proactive approach to environmental contaminant monitoring.

Authors: Cossaboon JM, Hoh E, Chivers SJ, Weller DW, Danil K, Maruya KA, Dodder NG.

Full Source: Chemosphere. 2019 Jan 7; 221:656-664. doi: 10.1016/j.chemosphere.2019.01.050. [Epub ahead of print]

In the present study, the authors selected five marine mammal species as possible indicators for the Southern California Bight (SCB) and applied a non-targeted analytical method paired with an automated data reduction strategy to catalogue compounds in their blubber.

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Fate and toxicity of spilled chemicals in groundwater and soil environment I: strong acids

2019-04-01

This study reviewed the chemical/physical properties, toxicity, environmental fate, and ecotoxicity of strong acids in soil and groundwater environments. It was recommended that sulfuric acid and hydrofluoric acid be classified as chemicals of priority control based on volumes used, toxicity, carcinogenicity, and past significant spill events. Understanding the behaviour and transport of spilled strong acids in soil and groundwater environments requires a multi-disciplinary approach, as they can undergo a variety of geochemical and biochemical reactions with complex geomedia. The toxicity of spilled acid is dependent on the characteristics of the geomedia exposed to the acid and the amount of residual protons following acid-substrate interaction. Soil texture, cation exchange capacity, mineral composition, bedrock type, and aluminium content may be important factors affecting the toxicity of spilled acid in soil-groundwater environments. The authors expect that the results of this study will contribute preliminary data for future research on chemical spills.

Authors: Shin D, Kim Y, Moon HS.

Full Source: Environmental Health & Toxicology. 2018 Dec;33(4): e2018019. doi: 10.5620/eht.e2018019. Epub 2018 Dec 13.

Grapevine Trunk Diseases: A Review of Fifteen Years of Trials for Their Control with Chemicals and Biocontrol Agents

2019-04-01

Grapevine trunk diseases (GTDs) represent one of the most important problems for viticulture worldwide. Beyond the original causes of this outbreak in some countries like France, the lack of efficient control protocols and the prohibition of using active ingredients such as sodium arsenite and benzimidazoles, until recently used to reduce the impact of some GTDs but deleterious for humans and the environment, have probably worsened the impact of the diseases, leading to increasing economic losses. Since 1990, searches have been made to find efficient tools to control GTDs, testing a wide range of active ingredients and biocontrol agents. This review provides an overview of the results reported in the scientific literature over the last 15 years. In particular, the review focuses on the trials carried out applying chemicals or microorganisms

This study reviewed the chemical/physical properties, toxicity, environmental fate, and ecotoxicity of strong acids in soil and groundwater environments.

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to control Esca complex diseases, *Botryosphaeria dieback*, and *Eutypa dieback*, the most widespread GTDs.

Authors: Mondello V, Songy A, Battiston E, Pinto C, Coppin C, Trotel-Aziz P, Clément C, Mugnai L, Fontaine F.

Full Source: *Plant Disease*. 2018 Jul; 102(7):1189-1217. doi: 10.1094/PDIS-08-17-1181-FE. Epub 2018 Jun 11.

Electro-driven methanogenic microbial community diversity and variability in the electron abundant niche

2019-04-01

The underlying dynamics of microbial (bacteria and archaea) communities ecologically responding to an applied potential are critical to achieving the goal of enhancing bioenergy recovery but are not sufficiently understood. In this study, the authors built a MEC-AD mode that increased methane production rate by several times (max. 3.8 times) during the start-up period compared to control AD, changed the absence or presence of external voltage to provide the pre-, dur-, and post-samples for microbial analysis. From a time and spatially dependent community analysis of electrode-respiring bacteria and methanogens, the corresponding *Geobacter* developed under the influence of external voltage, pairing with methanogens in the anodic and cathodic biofilm to generate methane. Additionally, at the cathode, the *Alkaliphilus* (basophilic bacteria) also correspondingly shifted alongside the change of external voltage. The *mcrA* sequencing confirmed a change in the dominant microbe from acetoclastic (mostly *Methanosarcina mazei* LYC) to hydrogenotrophic methanogens (mostly basophilic *Methanobacterium alcaliphilum*) at the cathode with 0.8 V voltage. Overall, the external voltage not only enriched the functional microbes including electrogens and methanogens but also indirectly shifted the composition of the bacterial and archaeal community via disturbing the pH condition. The predictive functional profiling indicated that the cathodic methanogenesis principally followed the metabolism pathway of the hydrogenotrophic methanogens, suggesting the F420 co-enzyme could be the key mediate for electron transfer. All data suggested that the electric stimulation would

In this study, the authors built a MEC-AD mode that increased methane production rate by several times

change and maintain the micro-environmental conditions to shift the bacterial/archaeal community.

Authors: Cai W, Liu W, Zhang Z, Feng K, Ren G, Pu C, Li J, Deng Y, Wang A.

Full Source: Science of the Total Environment. 2019 Apr 15; 661:178-186. doi: 10.1016/j.scitotenv.2019.01.131. Epub 2019 Jan 14.

Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) induce different modes of action in reproduction to Japanese medaka (*Oryzias latipes*)

2019-04-01

Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) have widely and frequently used in many industrial sectors, and thus have been frequently found in the environment. These chemicals may act as endocrine disrupting chemicals (EDCs), although the molecular mechanisms are still debated. In this study, Japanese medaka (*Oryzias latipes*) were exposed to 10 mg/l PFOA and 1 mg/l PFOS for 21 days, and the reproductive responses, such as the fecundity, secondary sexual characteristics and transcriptional levels of vitellogenin (vtg1 and vtg2) and choriogenin (chgh, chghm and chgl), were time-dependently evaluated (day 7, 14 and 21). PFOA and PFOS significantly reduced fecundity, and caused expression changes in the genes with time, although the patterns were different for each chemical and each sex. Different transcriptional regulations of vitellogenin and choriogenin in male suggest that PFOA and PFOS have different mode of actions in reproductive effects despite their similar chemical structure.

Authors: Kang JS, Ahn TG, Park JW.

Full Source: Journal of Hazardous Materials. 2019 Jan 14; 368:97-103. doi: 10.1016/j.jhazmat.2019.01.034. [Epub ahead of print]

The treatment of sarcoptic mange in wildlife: a systematic review.

2019-04-01

Sarcoptic mange, caused by the *Sarcoptes scabiei* mite, is an infectious disease of wildlife, domestic animals and humans with international importance. Whilst a variety of treatment and control methods have been investigated in wildlife, the literature is fragmented and lacking consensus. The primary objectives of this review were to synthesise the diverse

In this study, Japanese medaka (*Oryzias latipes*) were exposed to PFOA and PFOS and the reproductive responses were evaluated.

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literature published on the treatment of sarcoptic mange in wildlife from around the world, and to identify the qualities of successful treatment strategies in both captive and free-roaming wildlife. A systematic search of the electronic databases CAB Direct, PubMed, Scopus, Web of Science, EMBASE and Discovery was undertaken. Data pertaining to study design, country, year, species, study size, mange severity, treatment protocol and outcomes were extracted from eligible studies and placed in a table. Following data extraction, a decision tree was used to identify studies suitable for further analysis based on the effectiveness of their treatment protocol, whether they were conducted on captive or non-captive wildlife, and the quality of their post-treatment monitoring period. Twenty-eight studies met our initial inclusion criteria for data collection. Of these studies, 15 were selected for further analysis following application of the decision tree. This comprised of 9 studies on captive wildlife, 5 studies on free-living wildlife and 1 study involving both captive and free-living wildlife. Ivermectin delivered multiple times via subcutaneous injection at a dose between 200-400 µg/kg was found to be the most common and successfully used treatment, although long-term data on post-release survival and re-infection rates was elusive. To the authors knowledge, this review is the first to demonstrate that multiple therapeutic protocols exist for the treatment of sarcoptic mange in wildlife. However, several contemporary treatment options are yet to be formally reported in wildlife, such as the use of isoxazoline chemicals as a one-off treatment. There is also a strong indication for more randomised controlled trials, as well as improved methods of post-treatment monitoring. Advancing this field of knowledge is expected to aid veterinarians, wildlife workers and policy makers with the design and implementation of effective treatment and management strategies for the conservation of wildlife affected by sarcoptic mange.

Authors: Rowe ML, Whiteley PL, Carver S.

Full Source: Parasites & Vectors. 2019 Mar 13;12(1):99. doi: 10.1186/s13071-019-3340-z.

Oestrogenic action of chronic low-dose nonylphenol (NP) and di-(2-ethylhexyl) phthalate (DEHP) in mouse uterus was assessed in this study.

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MEDICAL RESEARCH

Chronic Low-Dose Nonylphenol or Di-(2-ethylhexyl) Phthalate has a Different Oestrogen-like Response in Mouse Uterus

2019-04-01

Through the development of organic synthetic skill, chemicals that mimic signalling mediators such as steroid hormones have been exposed to the environment. Recently, it has become apparent that this circumstance should be further studied in the field of physiology. Oestrogenic action of chronic low-dose nonylphenol (NP) and di-(2-ethylhexyl) phthalate (DEHP) in mouse uterus was assessed in this study. Ten to twelve-week-old female mice (CD-1) were fed drinking water containing NP (50 or 500 µg/L) or DEHP (133 or 1,330 µg/L) for 10 weeks. Uterine diameter, the thickness of myometrium and endometrium, and the height of luminal epithelial cells were measured and the number of glands were counted. The expression levels of the known 17β-oestradiol (E2)-regulated genes were evaluated with real-time RT-PCR methodology. The ration of uterine weight to body weight increased in 133 µg/L DEHP. Endometrial and myometrial thickness increased in 133 and 1,330 µg/L DEHP treated groups, and in 50, 500 µg/L NP and 133 µg/L DEHP, respectively. The height of luminal epithelial cell decreased in NP groups. The numbers of luminal epithelial gland were decreased in NP groups but increased in 50 µg/L DEHP group. The histological characters of glands were not different between groups. The mRNA expression profiles of the known 17β-oestradiol (E2) downstream genes, *Esr1*, *Esr2*, *Pgr*, *Lox*, and *Muc1*, were also different between NP and DEHP groups. The expression levels dramatically increased in some genes by the NP or DEHP. Based on these results, it is suggested that the chronic low-dose NP or DEHP works as oestrogen-like messengers in uterus with their own specific gene expression-regulation patterns.

Authors: Kim J, Cha S, Lee MY, Hwang YJ, Yang E, Ryou C, Jung HI, Cheon YP.

Full Source: Development & Reproduction. 2018 Dec;22(4):379-391. doi: 10.12717/DR.2018.22.4.379. Epub 2018 Dec 31.

The objectives of this study were to evaluate and compare treatment patterns and infusion-related health care resource expenditures for rheumatoid arthritis (RA) patients initiating golimumab for intravenous use (GLM-IV) and infliximab (IFX) therapy and to assess cost implications from the commercial perspective.

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Comparative analysis of US real-world dosing patterns and direct infusion-related costs for matched cohorts of rheumatoid arthritis patients treated with infliximab or intravenous golimumab

2019-04-01

The objectives of this study were to evaluate and compare treatment patterns and infusion-related health care resource expenditures for rheumatoid arthritis (RA) patients initiating golimumab for intravenous use (GLM-IV) and infliximab (IFX) therapy and to assess cost implications from the commercial perspective. Adult RA patients with a new episode of GLM-IV or IFX treatment between 1 January 2014 and 31 March 2016 were identified from MarketScan databases and evaluated for maintenance infusion intervals and related costs of treatment. IFX and GLM-IV patients were matched 1:1 on index medication treatment duration, gender, payer type, prior biologic use, and post-index methotrexate use. Paid amounts for drugs and associated administration costs were applied to treatment group dosing patterns. Final matched treatment groups included 547 GLM-IV and 547 IFX patients (mean age = 55-56 years). Mean (SD) follow-up was 609 (161) days for GLM-IV and 613 (163) days for IFX. Treatment duration was 396 (240) days for GLM-IV and 397 (239) days for IFX. Overall, 80% of GLM-IV and 39% of IFX maintenance infusions were given approximately every 8 weeks; and 6% of GLM-IV and 53% of IFX maintenance infusions occurred more frequently than every 8 weeks ($P < 0.001$). When weighting of the maintenance infusion interval was applied, the mean number of induction plus maintenance infusions during the first year of treatment was estimated at 7.03 for GLM-IV and 9.48 for IFX. From the commercial perspective, drug plus administration costs per infusion were \$5,846 for GLM-IV and \$5,444 for IFX with total annual cost of therapy for GLM-IV patients costing \$10,507 less than that for IFX patients in the first year and \$6,774 less than that for IFX patients in subsequent years. Annual GLM-IV drug plus administration costs for commercial health plans were significantly less than IFX in RA patients due to differences in real-world dosing and administration.

Authors: Ellis LA, Malangone-Monaco E, Varker H, Stetsovsky D, Kubacki M, DeHoratius RJ, Kafka S.

Full Source: ClinicoEconomics and Outcomes Research. 2019 Jan 15; 11:99-110. doi: 10.2147/CEOR.S185547. eCollection 2019.

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Cabozantinib as first-line treatment in advanced renal cell carcinoma: a profile of its use

2019-04-01

Oral cabozantinib tablets (Cabometyx®) are an important option for the treatment of advanced renal cell carcinoma (RCC). Cabozantinib is an anti-angiogenic agent and potently inhibits multiple tyrosine kinases, including those implicated in the development of RCC. The previously approved indication of cabozantinib tablets (i.e. treatment of advanced RCC following prior VEGF-targeted therapy) has been extended to include the first-line treatment of advanced RCC in treatment-naïve adults with intermediate or poor risk (EU) and all patients with advanced RCC (USA). These label extensions are based on the results of a randomised, open-label phase 2 trial, in which adults with metastatic RCC of poor or intermediate risk received targeted first-line treatment with cabozantinib or standard-of-care sunitinib. Relative to sunitinib, cabozantinib significantly prolonged median progression-free survival (primary endpoint; investigator and independent assessments), and increased the objective response rate (investigator assessment). The tolerability profile of cabozantinib is comparable to those of other tyrosine kinase inhibitors, with adverse events being manageable with medical intervention, dosage reductions, treatment interruption and/or permanent discontinuation.

Author: Lyseng-Williamson KA.

Full Source: *Drugs & Therapy Perspectives*. 2018;34(10):457-465. doi: 10.1007/s40267-018-0547-6. Epub 2018 Aug 7.

Initiation of Pulmonary Fibrosis after Silica Inhalation in Rats is linked with Dysfunctional Shelterin Complex and DNA Damage Response

2019-04-01

Occupational exposure to silica has been observed to cause pulmonary fibrosis and lung cancer through complex mechanisms. Telomeres, the nucleoprotein structures with repetitive (TTAGGG) sequences at the end of chromosomes, are a molecular “clock of life”, and alterations are associated with chronic disease. The shelterin complex (POT1, TRF1, TRF2, Tin2, Rap1, and POT1 and TPP1) plays an important role in maintaining telomere length and integrity, and any alteration in telomeres may activate DNA damage response (DDR) machinery resulting in telomere attrition. The goal of this study was to assess the effect of silica exposure on the regulation of the shelterin complex in an animal model. Male

The goal of this study was to assess the effect of silica exposure on the regulation of the shelterin complex in an animal model.

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Fisher 344 rats were exposed by inhalation to Min-U-Sil 5 silica for 3, 6, or 12 wk at a concentration of 15 mg/m³ for 6 hr/d for 5 consecutive d/wk. Expression of shelterin complex genes was assessed in the lungs at 16 hr after the end of each exposure. Also, the relationship between increased DNA damage protein (γ H2AX) and expression of silica-induced fibrotic marker, α SMA, was evaluated. The findings reveal new information about the dysregulation of shelterin complex after silica inhalation in rats, and how this pathway may lead to the initiation of silica-induced pulmonary fibrosis.

Authors: Shoeb M, Mustafa GM, Joseph P, Umbright C, Kodali V, Roach KA, Meighan T, Roberts JR, Erdely A, Antonini JM.

Full Source: Science Reports. 2019 Jan 24;9(1):471. doi: 10.1038/s41598-018-36712-6.

A randomised controlled trial of a mitochondrial therapeutic target for bipolar depression: mitochondrial agents, N-acetylcysteine, and placebo

2019-04-01

A phasic dysregulation of mitochondrial bioenergetics may operate in bipolar disorder, increased in mania and decreased in depression. In this study, the authors aimed to examine efficacy of two add-on treatments in bipolar depression: N-acetylcysteine (NAC) and NAC with a combination of nutraceutical agents that may increase mitochondrial biogenesis. A three-arm 16-week, double-blind, randomised, placebo-controlled trial, adjunctive to usual treatment, was conducted. Participants (n = 181) with bipolar disorder and current depressive symptoms were randomised to 2000 mg/day NAC (n = 59), 2000 mg/day NAC with the combination nutraceutical treatment (CT, n = 61), or placebo (n = 61). The primary outcome was change in Montgomery-Åsberg Depression Rating Scale (MADRS) total score from baseline to week 16. Young Mania Rating Scale, Clinical Global Impression (CGI)-Improvement and CGI-Severity scales, Patient Global Impression scale, Social and Occupational Functioning Assessment Scale (SOFAS), Longitudinal Interval Follow-Up Evaluation - Range of Impaired Functioning Tool (LIFE-RIFT), and Quality of Life Enjoyment, and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) were secondary outcomes. One hundred forty-eight participants had post-randomisation data and were analysed (NAC = 52, CT = 47, Placebo = 49). No between-group differences were found for the rate of change between baseline and 16 weeks on any of the clinical and functioning variables.

In this study, the authors aimed to examine efficacy of two add-on treatments in bipolar depression: N-acetylcysteine (NAC) and NAC with a combination of nutraceutical agents that may increase mitochondrial biogenesis.

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Improvements in MADRS, BDRS, SOFAS, and LIFE-RIFT scores from baseline to the week 20 post-discontinuation visit were significantly greater in the CT group compared to those in the placebo. At week 20, the CGI-I was significantly lower in the CT group versus placebo. Gastrointestinal symptoms were significantly greater in the NAC than in the placebo group. These overall negative results, with no significant differences between groups detected at the primary outcome but some positive secondary signals, suggest either delayed benefit of the combination or an improvement of symptoms on withdrawal which warrants further exploration regarding the composition, mechanisms, and application of mitochondrial agents in illnesses characterised by mitochondrial dysfunction.

Authors: Berk M, Turner A, Malhi GS, Ng CH, Cotton SM, Dodd S, Samuni Y, Tanious M, McAulay C, Dowling N, Sarris J, Owen L, Waterdrinker A, Smith D, Dean OM.

Full Source: BMC Medicine. 2019 Jan 25;17(1):18. doi: 10.1186/s12916-019-1257-1.

OCCUPATIONAL RESEARCH

Health Risks of Polybrominated Diphenyl Ethers (PBDEs) and Metals at Informal Electronic Waste Recycling Sites

2019-04-01

Concerns about the adverse public health consequences of informal electronic waste (e-waste) recycling are increasing. This study adopted a cross-sectional study design to gain insights into health risks (cancer and non-cancer risks) associated with exposure to e-waste chemicals among informal e-waste workers via three main routes: Dermal contact, ingestion, and inhalation. The e-waste chemicals (PBDE and metals) were measured in the dust and top soils at e-waste sites (burning, dismantling, and repair sites). Adverse health risks were calculated using the EPA model developed by the Environmental Protection Agency of the United States. The concentrations of the e-waste chemicals and the health risks at the e-waste sites increased as the intensity of the e-waste recycling activities increased: control sites < repair sites < dismantling sites < burning sites. Dermal contact was the main route of exposure while exposure via inhalation was negligible for both carcinogenic and non-carcinogenic risks. Cumulative health risks via all routes of exposure

This study adopted a cross-sectional study design to gain insights into health risks (cancer and non-cancer risks) associated with exposure to e-waste chemicals among informal e-waste workers via three main routes: Dermal contact, ingestion, and inhalation.

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(inhalation, ingestion, and dermal contact) exceeded the acceptable limits of both non-cancer effects and cancer risk at all e-waste sites. This indicates that overall the e-waste workers are at the risk of adverse health effects. Therefore, the importance of occupational safety programs and management regulations for e-waste workers cannot be over emphasised.

Authors: Ohajinwa CM, van Bodegom PM, Osibanjo O, Xie Q, Chen J, Vijver MG, Peijnenburg WJGM.

Full Source: International Journal of Environmental Research & Public Health. 2019 Mar 13;16(6). pii: E906. doi: 10.3390/ijerph16060906.

Visualised Networking of Co-Regulated Lipids in Human Blood Based on High-Throughput Screening Data: Implications for Exposure Assessment

2019-04-01

Exposure to environmental chemicals could disturb lipidome homeostasis in biotas. Comprehensive identification and interpretation of lipid molecules in biological samples are of great importance to elucidate the potential changes in lipid homeostasis upon exposure to various environmental stimuli. In this study, a total of 156 human blood samples were collected including 108 general citizens (control group) and 48 employees in a municipal solid waste incineration (MSWI) plant (occupational exposure group). More than 1500 lipid molecules, belonging to five lipid classes, were screened in the blood samples by UPLC-QTOF-MS in the MSE acquisition mode. All of the coupled compounds with correlation coefficients (R) of 0.7 or higher were selected for automated network correlation analysis. A global visual network was automatically produced from thousands of coregulated lipid species in the blood samples. In the automatically produced molecular network, the distributions of the major correlated lipids were in accordance with their metabolic pathways in the KEGG map. Different lipidomic profiles in the blood samples from the two groups of people were easily observed by this visualisation technique. Among the intrinsic lipid classes, glycerides and sterol lipids might represent the most sensitively affected lipids upon exposure to various pollutants emitted from the MSWI plant. The visualised network of coregulated lipids identified in human blood presents a new approach for interpreting the metabolic relationships

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among the thousands of metabolites identified in toxicological and epidemiological studies.

Authors: Gao S, Wan Y, Li W, Huang C.

Full Source: Environmental Science & Technology. 2019 Mar 5;53(5):2862-2872. doi: 10.1021/acs.est.8b06289. Epub 2019 Feb 21.

Association of occupational exposures with cardiovascular disease among US Hispanics/Latinos

2019-04-01

Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in the USA. The role of occupational exposures to chemicals in the development of CVD has rarely been studied even though many agents possess cardiotoxic properties. In the present study, the authors evaluated associations of self-reported exposures to organic solvents, metals and pesticides in relation to CVD prevalence among diverse Hispanic/Latino workers. Cross-sectional data from 7404 employed individuals, aged 18-74 years, enrolled in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) were analysed. Participants from four US cities provided questionnaire data and underwent clinical examinations, including ECGs. CVD was defined as the presence of at least one of the following: coronary heart disease, atrial fibrillation, heart failure or cerebrovascular disease. Prevalence ratios reflecting the relationship between each occupational exposure and CVD as well as CVD subtypes were calculated using Poisson regression models. Hispanic/Latino workers reported exposures to organic solvents (6.5%), metals (8.5%) and pesticides (4.7%) at their current jobs. Overall, 6.1% of participants had some form of CVD, with coronary heart disease as the most common (4.3%) followed by cerebrovascular disease (1.0%), heart failure (0.8%) and atrial fibrillation (0.7%). For individuals who reported working with pesticides, the prevalence ratios for any CVD were 2.18 (95% CI 1.34 to 3.55), coronary heart disease 2.20 (95% CI 1.31 to 3.71), cerebrovascular disease 1.38 (95% CI 0.62 3.03), heart failure 0.91 (95% CI 0.23 to 3.54) and atrial fibrillation 5.92 (95% CI 1.89 to 18.61) after adjustment for sociodemographic, acculturation, lifestyle and occupational characteristics. Metal exposures were associated with an almost fourfold (3.78, 95% CI 1.24 to 11.46) greater prevalence of atrial fibrillation. Null associations were observed for organic solvent exposures. The results suggest that working with metals and pesticides could be risk

In the present study, the authors evaluated associations of self-reported exposures to organic solvents, metals and pesticides in relation to CVD prevalence among diverse Hispanic/Latino workers.

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factors for CVD among Hispanic/Latino workers. Further work is needed to evaluate these relationships prospectively.

Authors: Bulka CM, Daviglius ML, Persky VW, Durazo-Arvizu RA, Lash JP, Elfassy T, Lee DJ, Ramos AR, Tarraf W, Argos M.

Full Source: Heart. 2019 Mar;105(6):439-448. doi: 10.1136/heartjnl-2018-313463. Epub 2018 Dec 11.

PUBLIC HEALTH RESEARCH

Green tobacco sickness: mecamylamine, varenicline, and nicotine vaccine as clinical research tools and potential therapeutics

2019-04-01

Green tobacco sickness occurs from transdermal absorption of chemicals from freshly harvested, green tobacco leaves. Signs and symptoms include nausea, vomiting, headache, and abdominal cramps. Prevalence has shifted from the United States and Europe to China, India, and Brazil. Worldwide 8 million individuals are afflicted, including women and children. Areas covered: Mecamylamine (Inversine[®], Vecamyl[®]), a nicotinic acetylcholine receptor (nAChR) antagonist, should be tested as a remedy for green tobacco sickness. Mecamylamine is approved as an oral tablet for the treatment of hypertension, is safe, and is off-patent. Mecamylamine attenuates many of the effects of nicotine and tobacco including seizures, thereby supporting its use as an effective pharmacotherapy for tobacco dependence. Varenicline (Chantix[®]) and cytisine (Tabex[®]) are low efficacy (i.e. intrinsic activity) nAChR agonists, are used as smoking cessation aids, and are viable options to test as remedies against green tobacco sickness. Nicotine immunisation strategies may provide further options for future testing. Efforts to demonstrate reversal and/or prevention of green tobacco sickness by mecamylamine will underscore the importance of nicotine in this illness and highlight a new medication for effective treatment of tobacco poisoning.

Author: McMahon LR.

Full Source: Expert Review of Clinical Pharmacology. 2019 Mar;12(3):189-195. doi: 10.1080/17512433.2019.1570844. Epub 2019 Jan 24.

Green tobacco sickness occurs from transdermal absorption of chemicals from freshly harvested, green tobacco leaves.

Technical

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Understanding skin absorption of common aldehyde vapours from exposure during hazardous material incidents

2019-04-01

The toxic release of aldehyde vapours during a hazardous material (HAZMAT) incident primarily results in respiratory concerns for the unprotected public. However, skin absorption may be an important concurrent exposure route that is poorly understood for this scenario. This study provides experimental data on the skin absorption properties of common aldehydes used in industry, including acetaldehyde, acrolein, benzaldehyde and formaldehyde, in gaseous or vapour form using an adapted in vitro technique. Two of the four tested aldehydes were found to penetrate the skin in appreciable amounts following 30-min exposure at HAZMAT relevant atmospheric concentrations: acetaldehyde ($5.29 \pm 3.24 \mu\text{g}/\text{cm}^2$) and formaldehyde ($3.45 \pm 2.58 \mu\text{g}/\text{cm}^2$). Whereas only low levels of acrolein ($0.480 \pm 0.417 \mu\text{g}/\text{cm}^2$) and benzaldehyde ($1.46 \pm 0.393 \mu\text{g}/\text{cm}^2$) skin penetration was noted. The aldehydes demonstrated differing levels of interaction with fabric. Formaldehyde and acetaldehyde adsorbed strongly to denim, whereas benzaldehyde and acrolein displayed no sink properties. However, denim was shown to be an initial protective barrier and reduced penetration outcomes for all aldehydes. This study provides important information to assist first responders and confirms the relevance of using physicochemical properties (e.g. solubility, molecular weight, partition coefficient) to predict skin permeation potential in the absence of empirical data during HAZMAT incidents involving different types of aldehydes.

Authors: Thredgold L, Gaskin S, Heath L, Pisaniello D, Logan M, Baxter C.

Full Source: Journal of Exposure Science & Environmental Epidemiology. 2019 Feb 15. doi: 10.1038/s41370-019-0127-4. [Epub ahead of print]

Identification of Sex-Specific Transcriptome Responses to Polychlorinated Biphenyls (PCBs)

2019-04-01

PCBs are classified as xenoestrogens and carcinogens and their health risks may be sex-specific. To identify potential sex-specific responses to PCB-exposure the authors established gene expression profiles in a population study subdivided into females and males. Gene expression profiles were determined in a study population consisting of 512 subjects from the EnviroGenomarkers project, 217 subjects who developed lymphoma and

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295 controls were selected in later life. Linear mixed models were ran in order to find associations between gene expression and exposure to PCBs, while correcting for confounders, in particular distribution of white blood cells (WBC), as well as random effects. The analysis was subdivided according to sex and development of lymphoma in later life. The changes in gene expression as a result of exposure to the six studied PCB congeners were sex- and WBC type specific. The relatively large number of genes that are significantly associated with PCB-exposure in the female subpopulation already indicates different biological response mechanisms to PCBs between the two sexes. The interaction analysis between different PCBs and WBCs provides only a small overlap between sexes. In males, cancer-related pathways and in females immune system-related pathways are identified in association with PCBs and WBCs. Future lymphoma cases and controls for both sexes show different responses to the interaction of PCBs with WBCs, suggesting a role of the immune system in PCB-related cancer development.

Authors: Espín-Pérez A, Hebels DGAJ, Kiviranta H, Rantakokko P, Georgiadis P, Botsivali M, Bergdahl IA, Palli D, Späth F, Johansson A, Chadeau-Hyam M, Kyrtopoulos SA, Kleinjans JCS, de Kok TCMC.

Full Source: Science Reports. 2019 Jan 24;9(1):746. doi: 10.1038/s41598-018-37449-y.

The role of exposure to phthalates in variations of anogenital distance: A systematic review and meta-analysis

2019-04-01

Environmental chemicals such as phthalate esters may have adverse effects on anogenital distance (AGD), but the evidence in both genders has not been reviewed systematically. The objective of the present study is to conduct a systematic review and meta-analysis of studies that analysed the relationship between exposure to phthalates and AGD. English papers published up to March 2018 were searched in PubMed, Scopus, Clarivate-Web of Science, and Google scholar. The authors applied fixed-effects models to calculate pooled beta coefficient [β]. In the case of heterogeneity, random-effects models were used. Using the comprehensive search strategies, 313 papers were identified and after screening, 10 of them were included in this study. In primary analyses, it was found that exposure to phthalates was not associated with short AGD ($\beta = -0.11$; 95% CI, -0.27, 0.06; $I^2 = 0\%$). However, results

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of subgroup analyses indicated that in boys, the sum of di-2-ethylhexyl phthalate (Σ DEHP) metabolites had significant association with the risk of shortened anopenile distance (AGDAP) ($\beta = -0.915$, 95% CI: 1.629,-0.2) and anoscrotal distance (AGDAS) ($\beta = -0.857$, 95% CI: 1.455,-0.26). In addition, urinary monobutyl phthalate (MBP), monoethyl phthalate (MEP), and monoisobutyl phthalate (MiBP) were associated with short AGDAP. It was also observed significant association between monobenzylphthalate (MBzP) and anofourchette distance (AGDAF) in girls. This study provided findings on significant association of exposure to Σ DEHP metabolites, MBP, MEP, and MiBP with shortened AGDAP in boys. The mechanisms of phthalates effect on AGD may involve receptors and enzymes involved in steroidogenesis, negative influence on Leydig cells, cell proliferation, gonocyte cell numbers, and testosterone production.

Authors: Zarean M, Keikha M, Feizi A, Kazemitabae M, Kelishadi R.

Full Source: Environmental Pollution. 2019 Jan 9; 247:172-179. doi: 10.1016/j.envpol.2019.01.026. [Epub ahead of print]

Spot Urine Sodium-to-Potassium Ratio Is a Predictor of Stroke

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Dietary sodium reduction with concurrent increase in potassium intake is a current public health priority to reduce risk of cardiovascular events. This study explored associations between the spot urine sodium-to-potassium ratio and cardiovascular events in the MESA (Multi-Ethnic Study of Atherosclerosis) longitudinal cohort. Methods- The MESA is a prospective cohort study of 6814 adults from 4 ethnic groups (European-, Asian-, African- and Hispanic-American) with a mean age of 62 (± 10.2) years and an average of 11.7 (± 2.2) years of follow-up. Participants were free of clinical cardiovascular disease at baseline. Spot urine sodium and potassium excretion, as a marker of dietary intake, was collected at baseline. The impact of urinary sodium-to-potassium ratio on adjudicated cardiovascular events was assessed using Cox proportional hazards models. Results- Only 39% of MESA participants had a urinary sodium-to-potassium ratio ≤ 1 , and these participants experienced only 74 of the 236 strokes. A sodium-to-potassium ratio > 1 was associated with a hazard ratio of 1.47 (95% CI, 1.07-2.00) for risk of stroke, adjusting for age, sex, race, cardiovascular risk factors, socio-demographic characteristics, body size, and kidney function. The spot urine sodium-to-potassium ratio (measurable in routine care) is associated with stroke. A urine sodium-to-

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potassium ratio of ≤ 1 , may be related to a clinically relevant reduction in stroke risk and is a feasible target for health interventions.

Authors: Averill MM, Young RL, Wood AC, Kurlak EO, Kramer H, Steffen L, McClelland RL, Delaney JA, Drewnowski A.

Full Source: Stroke. 2019 Feb;50(2):321-327. doi: 10.1161/STROKEAHA.118.023099.

Assessment of endocrine-disrupting activities of alternative chemicals for bis(2-ethylhexyl)phthalate

2019-04-01

Plastic products are closely intertwined with modern life. Some plasticisers used in making plastics, such as phthalates, are reported to be endocrine-disrupting chemicals. Plasticisers can be released into the environment, and health risks related to plasticiser exposure have been reported. In addition, due to plastic waste that flows into the ocean, microplastics have been found in marine products, including non-biological seawater products such as sea salt. Plastics can affect the body via a variety of pathways, and therefore safer alternative chemicals are needed.

Three chemicals were evaluated: acetyl tributyl citrate (ATBC), triethyl 2-acetyl citrate (ATEC), and trihexyl O-acetyl citrate (ATHC), replacing bis(2-ethylhexyl)phthalate (DEHP), a typical plasticizer. The endocrine-disrupting activities of each chemical, including estrogenic or anti-estrogenic activity (test guideline (TG) No. 455), androgenic or anti-androgenic activity (TG No. 458), steroidogenesis (TG No. 456), and oestrogenic properties via a short-term screening test using the uterotrophic assay (TG No. 440), were assessed in accordance with the Organisation for Economic Co-operation and Development guidelines for chemical testing. The results showed that DEHP, ATBC, ATEC, ATHC possess no oestrogenic activity, whereas DEHP, ATBC and ATHC demonstrate anti-estrogenic activity and ATBC anti-androgenic activity. DEHP and ATHC exhibited a disruption in steroidogenesis activities. Additional tests are necessary, but our results suggest that ATEC is a good candidate plasticizer providing a suitable alternative to DEHP.

Authors: Park J, Park C, Gye MC, Lee Y.

Full Source: Environmental Research. 2019 Feb 2; 172:10-17. doi: 10.1016/j.envres.2019.02.001. [Epub ahead of print]

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